

EXAMPLE 123: Isolation of cDNA clones Encoding Human PRO1287

An expressed sequence tag (EST) DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) was searched and an EST was identified which showed homology to the fringe protein. This EST sequence was then compared to various EST databases including public EST databases (e.g., GenBank), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify homologous EST sequences. The comparison was performed using the computer program BLAST or BLAST2 [Altschul et al., Methods in Enzymology, 266:460-480 (1996)]. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). This consensus sequence obtained is herein designated DNA40568.

Based on the DNA40568 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1287. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., Current Protocols in Molecular Biology, *supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

forward PCR primer 5'-CTCGGGAAAGGGACTTGATGTTGG-3' (SEQ ID NO:382)
reverse PCR primer 1 5'-GCGAAGGTGAGCCTATCTCGTGCC-3' (SEQ ID NO:383)
reverse PCR primer 2 5'-CAGCCTACACGTATTGAGG-3' (SEQ ID NO:384)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40568 sequence which had the following nucleotide sequence

hybridization probe

5'-CAGTCAGTACAATCCTGGCATAATACGGCCACCATGATGCAGTCCC-3' (SEQ ID NO:385).

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO1287 gene using the probe oligonucleotide and one of the PCR primers.

RNA for construction of the cDNA libraries was isolated from human bone marrow tissue. The cDNA libraries used to isolated the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a NotI site, linked with blunt to Sall hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRK5B or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., Science, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1287 (designated herein as DNA61755-1554 [Figure 275, SEQ ID NO:380]) and the derived protein sequence for PRO1287.

The entire nucleotide sequence of DNA61755-1554 is shown in Figure 275 (SEQ ID NO:380). The full length clone contained a single open reading frame with an apparent translational initiation site at nucleotide positions 655-657 and a stop signal at nucleotide positions 2251-2253 (Figure 275, SEQ ID NO:380). The predicted polypeptide precursor is 532 amino acids long, has a calculated molecular weight of approximately 61,351 daltons and an estimated pI of approximately 8.77. Analysis of the full-length PRO1287 sequence shown in Figure 276 (SEQ ID NO:381) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 27 and potential N-glycosylation sites from about amino acid 315 to about 5 amino acid 318 and from about amino acid 324 to about amino acid 327. Clone DNA61755-1554 has been deposited with ATCC on August 11, 1998 and is assigned ATCC deposit no. 203112.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 276 (SEQ ID NO:381), evidenced significant homology between the PRO1287 amino acid sequence and the following Dayhoff sequences: CET24D1_1, 10 EZRI_BOVIN, GGU19889_1, CC3_YEAST, S74244, NALS_MOUSE, MOES_PIG, S28660, S44860 and 15 YNA4_CAEEL.

EXAMPLE 124: Isolation of cDNA clones Encoding Human PRO1312

DNA55773 was identified in a human fetal kidney cDNA library using a yeast screen that 20 preferentially represents the 5' ends of the primary cDNA clones. Based on the DNA55773 sequence, oligonucleotides were synthesized for use as probes to isolate a clone of the full-length coding sequence for PRO1312.

The full length DNA61873-1574 clone shown in Figure 277 (SEQ ID NO:386) contained a single 25 open reading frame with an apparent translational initiation site at nucleotide positions 7-9 and ending at the stop codon found at nucleotide positions 643-645. The predicted polypeptide precursor is 212 amino acids long (Figure 278, SEQ ID NO:387). PRO1312 has a calculated molecular weight of approximately 24,024 daltons and an estimated pI of approximately 6.26. Other features include a signal peptide at about amino acids 1-14; a transmembrane domain at about amino acids 141-160, and potential N-glycosylation sites at about amino acids 76-79 and 93-96.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence 30 alignment analysis of the full-length sequence shown in Figure 278 (SEQ ID NO:387), revealed some homology between the PRO1312 amino acid sequence and the following Dayhoff sequences: GCINTALPH_1, GIBMUC1A_1, P_R96298, AF001406_1, PVU88874_1, P_R85151, AF041409_1, CELC50F2_7, C45875, and AB009510_21.

Clone DNA61873-1574 has been deposited with ATCC and is assigned ATCC deposit no. 203132.

EXAMPLE 125: Isolation of cDNA clones Encoding Human PRO1192

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is designated herein DNA35924. Based on the DNA35924 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1192.

5 PCR primers (forward and reverse) were synthesized:

forward PCR primer: 5'-CCGAGGCCATCTAGAGGCCAGAGC-3' (SEQ ID NO:390)

reverse PCR primer: 5'-ACAGGCAGAGCCAATGGCCAGAGC-3' (SEQ ID NO:391).

10 Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA35924 sequence which had the following nucleotide sequence:

hybridization probe:

5'-GAGAGGACTGCGGGAGTTGGGACCTTGTGCAGACGTGCTCATG-3' (SEQ ID NO:392).

15 In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1192 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver and spleen tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1192 designated herein as DNA62814-1521 and shown in Figure 279 (SEQ ID NO:388); and the derived protein sequence for PRO1192 which is shown in Figure 280 (SEQ ID NO:389).

20 The entire coding sequence of PRO1192 is shown in Figure 279 (SEQ ID NO:388). Clone DNA62814-1521 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and an apparent stop codon at nucleotide positions 766-768. The predicted polypeptide precursor is 215 amino acids long. The predicted polypeptide precursor has the following features: a signal peptide at about amino acids 1-21; a transmembrane domain at about amino acids 153-176; potential N-glycosylation sites at about amino acids 39-42 and 118-121; and homology with myelin P0 proteins at about amino acids 27-68 and 99-128 of Figure 280. The full-length PRO1192 protein shown in Figure 280 has an estimated molecular weight of about 24,484 daltons and a pI of about 6.98.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 280 (SEQ ID NO:389), revealed homology between the PRO1192 amino acid sequence and the following Dayhoff sequences: GEN12838, MYP0_HUMAN, AF049498_1, GEN14531, P_W14146, HS46KDA_1, CINB_RAT, OX2G_RAT, D87018_1, and D86996_2.

30 Clone DNA62814-1521 was deposited with the ATCC on August 4, 1998, and is assigned ATCC deposit no. 203093.

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EXAMPLE 126: Isolation of cDNA clones Encoding Human PRO1160

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described

in Example 1 above. This consensus sequence is herein designated DNA40650. Based on the DNA40650 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1160.

PCR primers (forward and reverse) were synthesized:

5 forward PCR primer 5'-GCTCCCTGATCTTCATGTCACCACC-3' (SEQ ID NO:395) .

reverse PCR primer 5'-CAGGGACACACTCTACCATCGGGAG-3' (SEQ ID NO:396)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA40650 sequence which had the following nucleotide sequence

hybridization probe

10 5'-CCATCTTCTGGTCTCTGCCAGAACAGCTGCTC-3' (SEQ ID NO:397)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1160 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast tissue.

15 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1160 (designated herein as DNA62872-1509 [Figure 281, SEQ ID NO: 393]) and the derived protein sequence for PRO1160.

The entire nucleotide sequence of DNA62872-1509 is shown in Figure 281 (SEQ ID NO:393). Clone 20 DNA62872-1509 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 40-42 and ending at the stop codon at nucleotide positions 310-312 (Figure 281). The predicted polypeptide precursor is 90 amino acids long (Figure 282). The full-length PRO1160 protein shown in Figure 282 has an estimated molecular weight of about 9,039 daltons and a pI of about 4.37. Analysis of the full-length PRO1160 sequence shown in Figure 282 (SEQ ID NO:394) evidences the presence of the following: 25 a signal peptide from about amino acid 1 to about amino acid 19 and a protein kinase C phosphorylation site from about amino acid 68 to about amino acid 70. Clone DNA62872-1509 has been deposited with ATCC on August 4, 1998 and is assigned ATCC deposit no. 203100.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 282 (SEQ ID NO:394), evidenced significant homology between the PRO1160 amino acid sequence and the following Dayhoff sequences: B30305, 30 GEN13490, I53641, S53363, HA34_BRELC, SP96_DICDI, S36326, SSU51197_10, MUC1_XENLA, TCU32448_1 and AF000409_1.

EXAMPLE 127: Isolation of cDNA clones Encoding Human PRO1187

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single 35 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing

homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57726.

5 In light of an observed sequence homology between the DNA57726 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 358563, the Incyte EST clone 358563 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 283 and is herein designated as DNA62876-1517.

10 The full length clone shown in Figure 283 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 121-123 and ending at the stop codon found at nucleotide positions 481-483 (Figure 283; SEQ ID NO:398). The predicted polypeptide precursor (Figure 284, SEQ ID NO:399) is 120 amino acids long. The signal peptide is at about amino acids 1-17 of SEQ ID NO:399. PRO1187 has a calculated molecular weight of approximately 12,925 daltons and an estimated pI of approximately 9.46. Clone DNA62876-1517 was deposited with the ATCC on August 4, 1998 and is assigned 15 ATCC deposit no. 203095. It is understood that the deposited clone contains the actual sequence and that the representations herein may have minor sequencing errors.

20 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 284 (SEQ ID NO:399), revealed some sequence identity (and therefore some relation) between the PRO1187 amino acid sequence and the following Dayhoff sequences: MGNENDOBX_1, CELF41G3_9, AMPG_STRLI, HSBBOVHERL_2, LEEXTEN10_1, AF029958_1 and P_W04957.

EXAMPLE 128: Isolation of cDNA clones Encoding Human PRO1185

25 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a 30 consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56426.

35 In light of an observed sequence homology between the DNA56426 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3284411, the Incyte EST clone 3284411 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 285 and is herein designated as DNA62881-1515.

The full length DNA62881-1515 clone shown in Figure 285 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 4-6 and ending at the stop codon found at nucleotide positions 598-600 (Figure 285; SEQ ID NO:400). The predicted polypeptide precursor (Figure 286, SEQ ID NO:401) is 198 amino acids long. The signal peptide is at about amino acids 1-21 of SEQ ID NO:401. PRO1185 has a calculated molecular weight of approximately 22,105 daltons and an estimated pI of approximately 7.73. Clone DNA62881-1515 has been deposited with the ATCC and is assigned ATCC deposit no. 203096.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 286 (SEQ ID NO:401), revealed some sequence identity between the PRO1185 amino acid sequence and the following Dayhoff sequences: TUP1_YEAST, AF041382_1, MAOM_SOLTU, SPPBPHU9_1, I41024, EPCPLCFAIL_1, HSPLC_1, YKL4_CAEEL, A44643, TGU65922_1.

EXAMPLE 129: Isolation of cDNA clones Encoding Human PRO1345

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA47364. Based on the DNA47364 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1345.

PCR primers (forward and reverse) were synthesized:
forward PCR primer 5'-CCTGGTTATCCCCAGGAACCTCCGAC-3' (SEQ ID NO:404)
reverse PCR primer 5'-CTCTTGCTGCTGCGACAGGCCTC-3' (SEQ ID NO:405)
Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA47364 sequence which had the following nucleotide sequence
hybridization probe
5'-CGCCCTCCAAGACTATGGTAAAAGGAGCCTGCCAGGTGTCAATGAC-3' (SEQ ID NO:406)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1345 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human breast carcinoma tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1345 (designated herein as DNA64852-1589 [Figure 287, SEQ ID NO:402]) and the derived protein sequence for PRO1345.

The entire nucleotide sequence of DNA64852-1589 is shown in Figure 287 (SEQ ID NO:402). Clone DNA64852-1589 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 7-9 or 34-36 and ending at the stop codon at nucleotide positions 625-627 (Figure 287). The predicted polypeptide precursor is 206 amino acids long (Figure 288). The full-length PRO1345 protein shown in Figure 288 has an estimated molecular weight of about 23,190 daltons and a pI of about 9.40. Analysis of

the full-length PRO1345 sequence shown in Figure 288 (SEQ ID NO:403) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 31 or from about amino acid 10 to about amino acid 31 and a C-type lectin domain signature sequence from about amino acid 176 to about amino acid 190. Clone DNA64852-1589 has been deposited with ATCC on August 18, 1998 and is assigned ATCC deposit no. 203127.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 288 (SEQ ID NO:403), evidenced significant homology between the PRO1345 amino acid sequence and the following Dayhoff sequences: BTU22298_1, TETN_CARSP, TETN_HUMAN, MABA_RAT, S34198, P_W13144, MACMBPA_1, A46274, PSPD_RAT AND P_R32188.

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EXAMPLE 130: Isolation of cDNA clones Encoding Human PRO1245

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56019.

In light of an observed sequence homology between the DNA56019 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 1327836, the Incyte EST clone 1327836 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 289 and is herein designated as DNA64884-1527.

25 The full length clone shown in Figure 289 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 79-81 and ending at the stop codon found at nucleotide positions 391-393 (Figure 289; SEQ ID NO:407). The predicted polypeptide precursor (Figure 290, SEQ ID NO:408) is 104 amino acids long, with a signal peptide sequence at about amino acid 1 to about amino acid 18. PRO1245 has a calculated molecular weight of approximately 10,100 daltons and an estimated pI of approximately 8.76.

30 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 290 (SEQ ID NO:408), revealed some homology between the PRO1245 amino acid sequence and the following Dayhoff sequences: SYA_THETH, GEN11167, MTV044_4, AB011151_1, RLAJ2750_3, SNELIPTRA_1, S63624, C28391, A37907, and 35 S14064.

Clone DNA64884-1245 was deposited with the ATCC on August 25, 1998 and is assigned ATCC deposit no. 203155.

EXAMPLE 131: Isolation of cDNA clones Encoding Human PRO1358

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

10 In light of an observed sequence homology between the consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 88718, the Incyte EST clone 88718 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 291 and is herein designated as DNA64890-1612.

15 The full length clone shown in Figure 291 contained a single open reading frame with an apparent translational initiation site at nucleotide positions 86 through 88 and ending at the stop codon found at nucleotide positions 1418 through 1420 (Figure 291; SEQ ID NO:409). The predicted polypeptide precursor (Figure 292, SEQ ID NO:410) is 444 amino acids long. The signal peptide is at about amino acids 1-18 of SEQ ID NO:410. PRO1358 has a calculated molecular weight of approximately 50,719 daltons and an estimated pI of approximately 8.82. Clone DNA64890-1612 was deposited with the ATCC on August 18, 20 1998 and is assigned ATCC deposit no. 203131.

25 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 292 (SEQ ID NO:410), revealed sequence identity between the PRO1358 amino acid sequence and the following Dayhoff sequences: P_W07607, AB000545_1, AB000546_1, A1AT_RAT, AB015164_1, P_P50021, COTR_CAVPO, and HAMHPP_1. The variants claimed in this application exclude these sequences.

EXAMPLE 132: Isolation of cDNA clones Encoding Human PRO1195

30 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a 35 consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA55716.

In light of an observed sequence homology between the DNA55716 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3252980, the Incyte EST clone 3252980 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 293 and is herein designated as DNA65412-1523.

The full length clone shown in Figure 293 contained a single open reading frame with an apparent 5 translational initiation site at nucleotide positions 58-60 and ending at the stop codon found at nucleotide positions 511-513 (Figure 293; SEQ ID NO:411). The predicted polypeptide precursor (Figure 294, SEQ ID NO:412) is 151 amino acids long. The signal sequence is at about amino acids 1-22 of SEQ ID NO:412. PRO1195 has a calculated molecular weight of approximately 17,277 daltons and an estimated pI of approximately 5.33. Clone DNA65412-1523 was deposited with the ATCC on August 4, 1998 and is assigned 10 ATCC deposit no. 203094.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence 15 alignment analysis of the full-length sequence shown in Figure 294 (SEQ ID NO:412), revealed some sequence identity between the PRO1195 amino acid sequence and the following Dayhoff sequences: MMU28486_1, AF044205_1, P_W31186, CELK03C7_1, F69034, EF1A_METVA, AF024540_1, SSU90353_1, MRSP_STAAU and P_R97680.

EXAMPLE 133: Isolation of cDNA clones Encoding Human PRO1270

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single 20 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 25 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57951.

In light of an observed sequence homology between the DNA57951 consensus sequence and an EST sequence encompassed within the Merck EST clone no. 124878, the Merck EST clone 124878 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. 30 The sequence of this cDNA insert is shown in Figure 295 and is herein designated as DNA66308-1537.

Clone DNA66308-1537 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 103-105 and ending at the stop codon at nucleotide positions 1042-1044 (Figure 295). The predicted polypeptide precursor is 313 amino acids long (Figure 296). The full-length PRO1270 35 protein shown in Figure 296 has an estimated molecular weight of about 34,978 daltons and a pI of about 5.71. Analysis of the full-length PRO1270 sequence shown in Figure 296 (SEQ ID NO:414) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 16, a potential N-glycosylation site from about amino acid 163 to about amino acid 166 and glycosaminoglycan attachment sites from about



amino acid 74 to about amino acid 77 and from about amino acid 289 to about amino acid 292. Clone DNA66308-1537 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203159.

5 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 296 (SEQ ID NO:414), evidenced significant homology between the PRO1270 amino acid sequence and the following Dayhoff sequences: XLU86699_1, S49589, FIBA_PARPA, FIBB_HUMAN, P_R47189, AF004326_1, DRTENASCN_1, AF004327_1, P_W01411 and FIBG_BOVIN.

EXAMPLE 134: Isolation of cDNA clones Encoding Human PRO1271

10 Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFSEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul 15 et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA57955.

20 In light of an observed sequence homology between the DNA57955 consensus sequence and an EST sequence encompassed within the Merck EST clone no. AA625350, the Merck EST clone AA625350 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 297 and is herein designated as DNA66309-1538.

25 Clone DNA66309-1538 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 94-96 and ending at the stop codon at nucleotide positions 718-720 (Figure 297). The predicted polypeptide precursor is 208 amino acids long (Figure 298). The full-length PRO1271 protein shown in Figure 298 has an estimated molecular weight of about 21,531 daltons and a pI of about 8.99. Analysis of the full-length PRO1271 sequence shown in Figure 298 (SEQ ID NO:416) evidences the presence 30 of the following: a signal peptide from about amino acid 1 to about amino acid 31 and a transmembrane domain from about amino acid 166 to about amino acid 187. Clone DNA66309-1538 has been deposited with ATCC on September 15, 1998 and is assigned ATCC deposit no. 203235.

35 An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 298 (SEQ ID NO:416), evidenced significant homology between the PRO1271 amino acid sequence and the following Dayhoff sequences: S57180, S63257, AGA1_YEAST, BPU43599_1, YS8A_CAEEL, S67570, LSU54556_2, S70305, VGLX_HSVEB, and D88733_1.

EXAMPLE 135: Isolation of cDNA clones Encoding Human PRO1375

A Merck/Wash. U. database was searched and a Merck EST was identified. This sequence was then put in a program which aligns it with other sequences from the Swiss-Prot public database, public EST databases (e.g., GenBank, Merck/Wash. U.), and a proprietary EST database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA). The search was performed using the computer program BLAST or BLAST2 [Altschul et al., *Methods in Enzymology*, 266:460-480 (1996)] as a comparison of the extracellular domain (ECD) protein sequences to a 6 frame translation of the EST sequences. Those comparisons resulting in a BLAST score of 70 (or in some cases, 90) or greater that did not encode known proteins were clustered and assembled into consensus DNA sequences with the program "phrap" (Phil Green, University of Washington, Seattle, Washington).

10 A consensus DNA sequence was assembled relative to other EST sequences using phrap. This consensus sequence is designated herein "DNA67003".

Based on the DNA67003 consensus sequence, the nucleic acid (SEQ ID NO:417) was identified in a human pancreas library. DNA sequencing of the clone gave the full-length DNA sequence for PRO1375 and the derived protein sequence for PRO1375.

15 The entire coding sequence of PRO1375 is shown in Figure 299 (SEQ ID NO:417). Clone DNA67004-1614 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 104-106 and an apparent stop codon at nucleotide positions 698-700 of SEQ ID NO:417. The predicted polypeptide precursor is 198 amino acids long. The transmembrane domains are at about amino acids 11-28 (type II) and 103-125 of SEQ ID NO:418. Clone DNA67004-1614 has been deposited with ATCC and 20 is assigned ATCC deposit no. 203115. The full-length PRO1375 protein shown in Figure 300 has an estimated molecular weight of about 22,531 daltons and a pI of about 8.47.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 300 (SEQ ID NO:418), revealed sequence identity between the PRO1375 amino acid sequence and the following Dayhoff sequences: AF026198_5, 25 CELR12C12_5, S73465, Y011_MYCPN, S64538_1, P_P8150, MUVSHPO10_1, VSH_MUMPL and CVU59751_5.

EXAMPLE 136: Isolation of cDNA clones Encoding Human PRO1385

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single 30 EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altschul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a 35 consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNAS7952.

In light of an observed sequence homology between the DNA57952 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3129630, the Incyte EST clone 3129630 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 301 and is herein designated as DNA68869-1610.

Clone DNA68869-1610 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 26-28 and ending at the stop codon at nucleotide positions 410-412 (Figure 301). The predicted polypeptide precursor is 128 amino acids long (Figure 302). The full-length PRO1385 protein shown in Figure 302 has an estimated molecular weight of about 13,663 daltons and a pI of about 10.97. Analysis of the full-length PRO1385 sequence shown in Figure 302 (SEQ ID NO:420) evidences the presence of the following: a signal peptide from about amino acid 1 to about amino acid 28, and glycosylaminoglycan attachment sites from about amino acid 82 to about amino acid 85 and from about amino acid 91 to about amino acid 94. Clone DNA68869-1610 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203164.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 302 (SEQ ID NO:420), evidenced low homology between the PRO1385 amino acid sequence and the following Dayhoff sequences: CELT14A8_1, LMNACHRA1_1, HXD9_HUMAN, CHKCMFL_1, HS5PP34_2, DMDRING_1, A37107_1, MMLUNGENE_1, PUM_DROME and DMU25117_1.

EXAMPLE 137: Isolation of cDNA clones Encoding Human PRO1387

Use of the signal sequence algorithm described in Example 3 above allowed identification of a single EST cluster sequence from the Incyte database. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., GenBank) and a proprietary EST DNA database (LIFESEQ®, Incyte Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA56259.

In light of an observed sequence homology between the DNA56259 consensus sequence and an EST sequence encompassed within the Incyte EST clone no. 3507924, the Incyte EST clone 3507924 was purchased and the cDNA insert was obtained and sequenced. It was found that this insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 303 and is herein designated as DNA68872-1620.

Clone DNA68872-1620 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 85-87 and ending at the stop codon at nucleotide positions 1267-1269 (Figure 303). The predicted polypeptide precursor is 394 amino acids long (Figure 304). The full-length PRO1387 protein shown in Figure 304 has an estimated molecular weight of about 44,339 daltons and a pI of about 7.10. Analysis of the full-length PRO1387 sequence shown in Figure 304 (SEQ ID NO:422) evidences the presence

of the following: a signal peptide from about amino acid 1 to about amino acid 19, a transmembrane domain from about amino acid 275 to about amino acid 296, potential N-glycosylation sites from about amino acid 76 to about amino acid 79, from about amino acid 231 to about amino acid 234, from about amino acid 302 to about amino acid 305, from about amino acid 307 to about amino acid 310 and from about amino acid 376 to about amino acid 379, and amino acid sequence blocks having homology to myelin p0 protein from about 5 amino acid 210 to about amino acid 239 and from about amino acid 92 to about amino acid 121. Clone DNA68872-1620 has been deposited with ATCC on August 25, 1998 and is assigned ATCC deposit no. 203160.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 304 (SEQ ID NO:422), evidenced significant 10 homology between the PRO1387 amino acid sequence and the following Dayhoff sequences: P_W36955, MYP0_HETFR, HS46KDA_1, AF049498_1, MYO0_HUMAN, AF030454_1, AS3268, SHPTCRA_1, P_W14146 and GEN12838.

EXAMPLE 138: Isolation of cDNA clones Encoding Human PRO1384

15 A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA54192. Based on the DNA54192 sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO1384.

PCR primers (forward and reverse) were synthesized:

20 forward PCR primer 5'-TGCAGCCCCGTGACACAACTGG-3' (SEQ ID NO:425)

reverse PCR primer 5'-CTGAGATAACCGAGCCATCCTCCAC-3' (SEQ ID NO:426)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the DNA54192 sequence which had the following nucleotide sequence:

hybridization probe

25 5'-GGAGATAGCTGCTATGGGTTCTTCAGGCACAACTTAACATGGGAAG-3' (SEQ ID NO:427)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used to isolate clones encoding the PRO1384 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal liver.

30 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO1384 (designated herein as DNA71159-1617 [Figure 305, SEQ ID NO:423]; and the derived protein sequence for PRO1384.

The entire coding sequence of PRO1384 is shown in Figure 305 (SEQ ID NO:423). Clone 35 DNA71159-1617 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 182-184 and an apparent stop codon at nucleotide positions 869-871. The predicted polypeptide precursor is 229 amino acids long. The full-length PRO1384 protein shown in Figure 306 has an estimated molecular weight of about 26,650 daltons and a pI of about 8.76. Additional features include a type II

transmembrane domain at about amino acids 32-57, and potential N-glycosylation sites at about amino acids 68-71, 120-123, and 134-137.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using a WU-BLAST2 sequence alignment analysis of the full-length sequence shown in Figure 306 (SEQ ID NO:424), revealed homology between the PRO1384 amino acid sequence and the following Dayhoff sequences: AF054819_1, HSAJ1687_1, AF009511_1, AB010710_1, GEN13595, HSAJ673_1, GEN13961, AB005900_1, LECH_CHICK, AF021349_1, and NK13_RAT.

Clone DNA71159-1617 has been deposited with ATCC and is assigned ATCC deposit no. 203135.

EXAMPLE 139: Use of PRO as a hybridization probe

10 The following method describes use of a nucleotide sequence encoding PRO as a hybridization probe.

DNA comprising the coding sequence of full-length or mature PRO as disclosed herein is employed as a probe to screen for homologous DNAs (such as those encoding naturally-occurring variants of PRO) in human tissue cDNA libraries or human tissue genomic libraries.

15 Hybridization and washing of filters containing either library DNAs is performed under the following high stringency conditions. Hybridization of radiolabeled PRO-derived probe to the filters is performed in a solution of 50% formamide, 5x SSC, 0.1% SDS, 0.1% sodium pyrophosphate, 50 mM sodium phosphate, pH 6.8, 2x Denhardt's solution, and 10% dextran sulfate at 42°C for 20 hours. Washing of the filters is performed in an aqueous solution of 0.1x SSC and 0.1% SDS at 42°C.

20 DNAs having a desired sequence identity with the DNA encoding full-length native sequence PRO can then be identified using standard techniques known in the art.

EXAMPLE 140: Expression of PRO in *E. coli*

This example illustrates preparation of an unglycosylated form of PRO by recombinant expression in *E. coli*.

25 The DNA sequence encoding PRO is initially amplified using selected PCR primers. The primers should contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector. A variety of expression vectors may be employed. An example of a suitable vector is pBR322 (derived from *E. coli*; see Bolivar et al., *Gene*, 2:95 (1977)) which contains genes for ampicillin and tetracycline resistance. The vector is digested with restriction enzyme and dephosphorylated. The PCR 30 amplified sequences are then ligated into the vector. The vector will preferably include sequences which encode for an antibiotic resistance gene, a trp promoter, a polyhis leader (including the first six STII codons, polyhis sequence, and enterokinase cleavage site), the PRO coding region, lambda transcriptional terminator, and an argU gene.

35 The ligation mixture is then used to transform a selected *E. coli* strain using the methods described in Sambrook et al., *supra*. Transformants are identified by their ability to grow on LB plates and antibiotic resistant colonies are then selected. Plasmid DNA can be isolated and confirmed by restriction analysis and DNA sequencing.

Selected clones can be grown overnight in liquid culture medium such as LB broth supplemented with antibiotics. The overnight culture may subsequently be used to inoculate a larger scale culture. The cells are then grown to a desired optical density, during which the expression promoter is turned on.

After culturing the cells for several more hours, the cells can be harvested by centrifugation. The cell pellet obtained by the centrifugation can be solubilized using various agents known in the art, and the 5 solubilized PRO protein can then be purified using a metal chelating column under conditions that allow tight binding of the protein.

PRO may be expressed in *E. coli* in a poly-His tagged form, using the following procedure. The DNA encoding PRO is initially amplified using selected PCR primers. The primers will contain restriction enzyme sites which correspond to the restriction enzyme sites on the selected expression vector, and other 10 useful sequences providing for efficient and reliable translation initiation, rapid purification on a metal chelation column, and proteolytic removal with enterokinase. The PCR-amplified, poly-His tagged sequences are then ligated into an expression vector, which is used to transform an *E. coli* host based on strain 52 (W3110 fuhA(tonA) lon galE rpoHts(htpRts) clpP(lacIq)). Transformants are first grown in LB containing 50 mg/ml carbenicillin at 30°C with shaking until an O.D.600 of 3-5 is reached. Cultures are then diluted 50-100 fold 15 into CRAP media (prepared by mixing 3.57 g (NH₄)₂SO₄, 0.71 g sodium citrate•2H₂O, 1.07 g KCl, 5.36 g Difco yeast extract, 5.36 g Sheffield hycase SF in 500 mL water, as well as 110 mM MPOS, pH 7.3, 0.55% (w/v) glucose and 7 mM MgSO₄) and grown for approximately 20-30 hours at 30°C with shaking. Samples are removed to verify expression by SDS-PAGE analysis, and the bulk culture is centrifuged to pellet the cells. Cell pellets are frozen until purification and refolding.

20 *E. coli* paste from 0.5 to 1 L fermentations (6-10 g pellets) is resuspended in 10 volumes (w/v) in 7 M guanidine, 20 mM Tris, pH 8 buffer. Solid sodium sulfite and sodium tetrathionate is added to make final concentrations of 0.1M and 0.02 M, respectively, and the solution is stirred overnight at 4°C. This step results in a denatured protein with all cysteine residues blocked by sulfitolization. The solution is centrifuged at 40,000 rpm in a Beckman Ultracentrifuge for 30 min. The supernatant is diluted with 3-5 volumes of metal chelate 25 column buffer (6 M guanidine, 20 mM Tris, pH 7.4) and filtered through 0.22 micron filters to clarify. The clarified extract is loaded onto a 5 ml Qiagen Ni-NTA metal chelate column equilibrated in the metal chelate column buffer. The column is washed with additional buffer containing 50 mM imidazole (Calbiochem, Utrol grade), pH 7.4. The protein is eluted with buffer containing 250 mM imidazole. Fractions containing the desired protein are pooled and stored at 4°C. Protein concentration is estimated by its absorbance at 280 nm 30 using the calculated extinction coefficient based on its amino acid sequence.

The proteins are refolded by diluting the sample slowly into freshly prepared refolding buffer consisting of: 20 mM Tris, pH 8.6, 0.3 M NaCl, 2.5 M urea, 5 mM cysteine, 20 mM glycine and 1 mM EDTA. Refolding volumes are chosen so that the final protein concentration is between 50 to 100 micrograms/ml. The refolding solution is stirred gently at 4°C for 12-36 hours. The refolding reaction is 35 quenched by the addition of TFA to a final concentration of 0.4% (pH of approximately 3). Before further purification of the protein, the solution is filtered through a 0.22 micron filter and acetonitrile is added to 2-10% final concentration. The refolded protein is chromatographed on a Poros R1/H reversed phase column

using a mobile buffer of 0.1% TFA with elution with a gradient of acetonitrile from 10 to 80%. Aliquots of fractions with A280 absorbance are analyzed on SDS polyacrylamide gels and fractions containing homogeneous refolded protein are pooled. Generally, the properly refolded species of most proteins are eluted at the lowest concentrations of acetonitrile since those species are the most compact with their hydrophobic interiors shielded from interaction with the reversed phase resin. Aggregated species are usually eluted at 5 higher acetonitrile concentrations. In addition to resolving misfolded forms of proteins from the desired form, the reversed phase step also removes endotoxin from the samples.

Fractions containing the desired folded PRO polypeptide are pooled and the acetonitrile removed using a gentle stream of nitrogen directed at the solution. Proteins are formulated into 20 mM Hepes, pH 6.8 with 0.14 M sodium chloride and 4% mannitol by dialysis or by gel filtration using G25 Superfine (Pharmacia) 10 resins equilibrated in the formulation buffer and sterile filtered.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 141: Expression of PRO in mammalian cells

This example illustrates preparation of a potentially glycosylated form of PRO by recombinant 15 expression in mammalian cells.

The vector, pRK5 (see EP 307,247, published March 15, 1989), is employed as the expression vector. Optionally, the PRO DNA is ligated into pRK5 with selected restriction enzymes to allow insertion of the PRO DNA using ligation methods such as described in Sambrook et al., *supra*. The resulting vector is called pRK5-PRO.

20 In one embodiment, the selected host cells may be 293 cells. Human 293 cells (ATCC CCL 1573) are grown to confluence in tissue culture plates in medium such as DMEM supplemented with fetal calf serum and optionally, nutrient components and/or antibiotics. About 10 μ g pRK5-PRO DNA is mixed with about 1 μ g DNA encoding the VA RNA gene [Thimmappaya et al., *Cell*, 31:543 (1982)] and dissolved in 500 μ l of 1 mM Tris-HCl, 0.1 mM EDTA, 0.227 M CaCl₂. To this mixture is added, dropwise, 500 μ l of 50 mM 25 HEPES (pH 7.35), 280 mM NaCl, 1.5 mM NaPO₄, and a precipitate is allowed to form for 10 minutes at 25°C. The precipitate is suspended and added to the 293 cells and allowed to settle for about four hours at 37°C. The culture medium is aspirated off and 2 ml of 20% glycerol in PBS is added for 30 seconds. The 293 cells are then washed with serum free medium, fresh medium is added and the cells are incubated for about 5 days.

30 Approximately 24 hours after the transfections, the culture medium is removed and replaced with culture medium (alone) or culture medium containing 200 μ Ci/ml ³⁵S-cysteine and 200 μ Ci/ml ³⁵S-methionine. After a 12 hour incubation, the conditioned medium is collected, concentrated on a spin filter, and loaded onto a 15% SDS gel. The processed gel may be dried and exposed to film for a selected period of time to reveal the presence of PRO polypeptide. The cultures containing transfected cells may undergo further incubation 35 (in serum free medium) and the medium is tested in selected bioassays.

In an alternative technique, PRO may be introduced into 293 cells transiently using the dextran sulfate method described by Sompanyrac et al., *Proc. Natl. Acad. Sci.*, 78:7575 (1981). 293 cells are grown to

maximal density in a spinner flask and 700 μ g pRK5-PRO DNA is added. The cells are first concentrated from the spinner flask by centrifugation and washed with PBS. The DNA-dextran precipitate is incubated on the cell pellet for four hours. The cells are treated with 20% glycerol for 90 seconds, washed with tissue culture medium, and re-introduced into the spinner flask containing tissue culture medium, 5 μ g/ml bovine insulin and 0.1 μ g/ml bovine transferrin. After about four days, the conditioned media is centrifuged and filtered to remove cells and debris. The sample containing expressed PRO can then be concentrated and purified by any selected method, such as dialysis and/or column chromatography.

5 In another embodiment, PRO can be expressed in CHO cells. The pRK5-PRO can be transfected into CHO cells using known reagents such as CaPO₄ or DEAE-dextran. As described above, the cell cultures can be incubated, and the medium replaced with culture medium (alone) or medium containing a radiolabel such 10 as ³⁵S-methionine. After determining the presence of PRO polypeptide, the culture medium may be replaced with serum free medium. Preferably, the cultures are incubated for about 6 days, and then the conditioned medium is harvested. The medium containing the expressed PRO can then be concentrated and purified by any selected method.

15 Epitope-tagged PRO may also be expressed in host CHO cells. The PRO may be subcloned out of the pRK5 vector. The subclone insert can undergo PCR to fuse in frame with a selected epitope tag such as a poly-his tag into a Baculovirus expression vector. The poly-his tagged PRO insert can then be subcloned into a SV40 driven vector containing a selection marker such as DHFR for selection of stable clones. Finally, the CHO cells can be transfected (as described above) with the SV40 driven vector. Labeling may be performed, as described above, to verify expression. The culture medium containing the expressed poly-His 20 tagged PRO can then be concentrated and purified by any selected method, such as by Ni²⁺-chelate affinity chromatography.

PRO may also be expressed in CHO and/or COS cells by a transient expression procedure or in CHO cells by another stable expression procedure.

25 Stable expression in CHO cells is performed using the following procedure. The proteins are expressed as an IgG construct (immunoadhesin), in which the coding sequences for the soluble forms (e.g. extracellular domains) of the respective proteins are fused to an IgG1 constant region sequence containing the hinge, CH2 and CH2 domains and/or is a poly-His tagged form.

30 Following PCR amplification, the respective DNAs are subcloned in a CHO expression vector using standard techniques as described in Ausubel et al., Current Protocols of Molecular Biology, Unit 3.16, John Wiley and Sons (1997). CHO expression vectors are constructed to have compatible restriction sites 5' and 3' of the DNA of interest to allow the convenient shuttling of cDNA's. The vector used expression in CHO cells is as described in Lucas et al., Nucl. Acids Res. 24:9 (1774-1779 (1996), and uses the SV40 early promoter/enhancer to drive expression of the cDNA of interest and dihydrofolate reductase (DHFR). DHFR expression permits selection for stable maintenance of the plasmid following transfection.

35 Twelve micrograms of the desired plasmid DNA is introduced into approximately 10 million CHO cells using commercially available transfection reagents Superfect[®] (Quiagen), Dospel[®] or Fugene[®] (Boehringer Mannheim). The cells are grown as described in Lucas et al., supra. Approximately 3 x 10⁷ cells are frozen

in an ampule for further growth and production as described below.

The ampules containing the plasmid DNA are thawed by placement into water bath and mixed by vortexing. The contents are pipetted into a centrifuge tube containing 10 mLs of media and centrifuged at 1000 rpm for 5 minutes. The supernatant is aspirated and the cells are resuspended in 10 mL of selective media (0.2 μ m filtered PS20 with 5% 0.2 μ m diafiltered fetal bovine serum). The cells are then aliquoted into a 100 mL spinner containing 90 mL of selective media. After 1-2 days, the cells are transferred into a 250 mL spinner filled with 150 mL selective growth medium and incubated at 37°C. After another 2-3 days, 250 mL, 500 mL and 2000 mL spinners are seeded with 3×10^5 cells/mL. The cell media is exchanged with fresh media by centrifugation and resuspension in production medium. Although any suitable CHO media may be employed, a production medium described in U.S. Patent No. 5,122,469, issued June 16, 1992 may actually be used.

10 A 3L production spinner is seeded at 1.2×10^6 cells/mL. On day 0, the cell number pH is determined. On day 1, the spinner is sampled and sparging with filtered air is commenced. On day 2, the spinner is sampled, the temperature shifted to 33°C, and 30 mL of 500 g/L glucose and 0.6 mL of 10% antifoam (e.g., 35% polydimethylsiloxane emulsion, Dow Corning 365 Medical Grade Emulsion) taken. Throughout the production, the pH is adjusted as necessary to keep it at around 7.2. After 10 days, or until the viability 15 dropped below 70%, the cell culture is harvested by centrifugation and filtering through a 0.22 μ m filter. The filtrate was either stored at 4°C or immediately loaded onto columns for purification.

For the poly-His tagged constructs, the proteins are purified using a Ni-NTA column (Qiagen). Before purification, imidazole is added to the conditioned media to a concentration of 5 mM. The conditioned media is pumped onto a 6 ml Ni-NTA column equilibrated in 20 mM Hepes, pH 7.4, buffer containing 0.3 20 M NaCl and 5 mM imidazole at a flow rate of 4-5 mL/min. at 4°C. After loading, the column is washed with additional equilibration buffer and the protein eluted with equilibration buffer containing 0.25 M imidazole. The highly purified protein is subsequently desalting into a storage buffer containing 10 mM Hepes, 0.14 M NaCl and 4% mannitol, pH 6.8, with a 25 mL G25 Superfine (Pharmacia) column and stored at -80°C.

25 Immunoadhesin (Fc-containing) constructs are purified from the conditioned media as follows. The conditioned medium is pumped onto a 5 mL Protein A column (Pharmacia) which had been equilibrated in 20 mM Na phosphate buffer, pH 6.8. After loading, the column is washed extensively with equilibration buffer before elution with 100 mM citric acid, pH 3.5. The eluted protein is immediately neutralized by collecting 1 mL fractions into tubes containing 275 μ L of 1 M Tris buffer, pH 9. The highly purified protein is subsequently desalting into storage buffer as described above for the poly-His tagged proteins. The homogeneity 30 is assessed by SDS polyacrylamide gels and by N-terminal amino acid sequencing by Edman degradation.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 142: Expression of PRO in Yeast

The following method describes recombinant expression of PRO in yeast.

35 First, yeast expression vectors are constructed for intracellular production or secretion of PRO from the ADH2/GAPDH promoter. DNA encoding PRO and the promoter is inserted into suitable restriction enzyme sites in the selected plasmid to direct intracellular expression of PRO. For secretion, DNA encoding

PRO can be cloned into the selected plasmid, together with DNA encoding the ADH2/GAPDH promoter, a native PRO signal peptide or other mammalian signal peptide, or, for example, a yeast alpha-factor or invertase secretory signal/leader sequence, and linker sequences (if needed) for expression of PRO.

Yeast cells, such as yeast strain AB110, can then be transformed with the expression plasmids described above and cultured in selected fermentation media. The transformed yeast supernatants can be analyzed by precipitation with 10% trichloroacetic acid and separation by SDS-PAGE, followed by staining of the gels with Coomassie Blue stain.

Recombinant PRO can subsequently be isolated and purified by removing the yeast cells from the fermentation medium by centrifugation and then concentrating the medium using selected cartridge filters. The concentrate containing PRO may further be purified using selected column chromatography resins.

10 Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 143: Expression of PRO in Baculovirus-Infected Insect Cells

The following method describes recombinant expression of PRO in Baculovirus-infected insect cells.

15 The sequence coding for PRO is fused upstream of an epitope tag contained within a baculovirus expression vector. Such epitope tags include poly-his tags and immunoglobulin tags (like Fc regions of IgG). A variety of plasmids may be employed, including plasmids derived from commercially available plasmids such as pVL1393 (Novagen). Briefly, the sequence encoding PRO or the desired portion of the coding sequence of PRO such as the sequence encoding the extracellular domain of a transmembrane protein or the sequence encoding the mature protein if the protein is extracellular is amplified by PCR with primers complementary 20 to the 5' and 3' regions. The 5' primer may incorporate flanking (selected) restriction enzyme sites. The product is then digested with those selected restriction enzymes and subcloned into the expression vector.

Recombinant baculovirus is generated by co-transfected the above plasmid and BaculoGold™ virus DNA (Pharmingen) into *Spodoptera frugiperda* ("Sf9") cells (ATCC CRL 1711) using lipofectin (commercially available from GIBCO-BRL). After 4 - 5 days of incubation at 28°C, the released viruses are harvested and used for further amplifications. Viral infection and protein expression are performed as described by O'Reilly et al., Baculovirus expression vectors: A Laboratory Manual, Oxford: Oxford University Press (1994).

30 Expressed poly-his tagged PRO can then be purified, for example, by Ni²⁺-chelate affinity chromatography as follows. Extracts are prepared from recombinant virus-infected Sf9 cells as described by Rupert et al., Nature, 362:175-179 (1993). Briefly, Sf9 cells are washed, resuspended in sonication buffer (25 mL Hepes, pH 7.9; 12.5 mM MgCl₂; 0.1 mM EDTA; 10% glycerol; 0.1% NP-40; 0.4 M KCl), and sonicated twice for 20 seconds on ice. The sonicates are cleared by centrifugation, and the supernatant is diluted 50-fold in loading buffer (50 mM phosphate, 300 mM NaCl, 10% glycerol, pH 7.8) and filtered through a 0.45 μm filter. A Ni²⁺-NTA agarose column (commercially available from Qiagen) is prepared with a bed volume of 5 mL, washed with 25 mL of water and equilibrated with 25 mL of loading buffer. The filtered cell extract is loaded onto the column at 0.5 mL per minute. The column is washed to baseline A₂₈₀ with loading buffer, at which point fraction collection is started. Next, the column is washed with a secondary wash buffer (50 mM phosphate; 300 mM NaCl, 10% glycerol, pH 6.0), which elutes nonspecifically bound

protein. After reaching A_{280} baseline again, the column is developed with a 0 to 500 mM Imidazole gradient in the secondary wash buffer. One mL fractions are collected and analyzed by SDS-PAGE and silver staining or Western blot with Ni^{2+} -NTA-conjugated to alkaline phosphatase (Qiagen). Fractions containing the eluted His₁₀-tagged PRO are pooled and dialyzed against loading buffer.

5 Alternatively, purification of the IgG tagged (or Fc tagged) PRO can be performed using known chromatography techniques, including for instance, Protein A or protein G column chromatography.

Many of the PRO polypeptides disclosed herein were successfully expressed as described above.

EXAMPLE 144: Preparation of Antibodies that Bind PRO

This example illustrates preparation of monoclonal antibodies which can specifically bind PRO.
10 Techniques for producing the monoclonal antibodies are known in the art and are described, for instance, in Goding, *supra*. Immunogens that may be employed include purified PRO, fusion proteins containing PRO, and cells expressing recombinant PRO on the cell surface. Selection of the immunogen can be made by the skilled artisan without undue experimentation.

15 Mice, such as Balb/c, are immunized with the PRO immunogen emulsified in complete Freund's adjuvant and injected subcutaneously or intraperitoneally in an amount from 1-100 micrograms. Alternatively, the immunogen is emulsified in MPL-TDM adjuvant (Ribi Immunochemical Research, Hamilton, MT) and injected into the animal's hind foot pads. The immunized mice are then boosted 10 to 12 days later with additional immunogen emulsified in the selected adjuvant. Thereafter, for several weeks, the mice may also be boosted with additional immunization injections. Serum samples may be periodically obtained from the 20 mice by retro-orbital bleeding for testing in ELISA assays to detect anti-PRO antibodies.

25 After a suitable antibody titer has been detected, the animals "positive" for antibodies can be injected with a final intravenous injection of PRO. Three to four days later, the mice are sacrificed and the spleen cells are harvested. The spleen cells are then fused (using 35% polyethylene glycol) to a selected murine myeloma cell line such as P3X63AgU.1, available from ATCC, No. CRL 1597. The fusions generate hybridoma cells which can then be plated in 96 well tissue culture plates containing HAT (hypoxanthine, aminopterin, and thymidine) medium to inhibit proliferation of non-fused cells, myeloma hybrids, and spleen cell hybrids.

30 The hybridoma cells will be screened in an ELISA for reactivity against PRO. Determination of "positive" hybridoma cells secreting the desired monoclonal antibodies against PRO is within the skill in the art.

35 The positive hybridoma cells can be injected intraperitoneally into syngeneic Balb/c mice to produce ascites containing the anti-PRO monoclonal antibodies. Alternatively, the hybridoma cells can be grown in tissue culture flasks or roller bottles. Purification of the monoclonal antibodies produced in the ascites can be accomplished using ammonium sulfate precipitation, followed by gel exclusion chromatography. Alternatively, affinity chromatography based upon binding of antibody to protein A or protein G can be employed.

EXAMPLE 145: Purification of PRO Polypeptides Using Specific Antibodies

Native or recombinant PRO polypeptides may be purified by a variety of standard techniques in the

art of protein purification. For example, pro-PRO polypeptide, mature PRO polypeptide, or pre-PRO polypeptide is purified by immunoaffinity chromatography using antibodies specific for the PRO polypeptide of interest. In general, an immunoaffinity column is constructed by covalently coupling the anti-PRO polypeptide antibody to an activated chromatographic resin.

5 Polyclonal immunoglobulins are prepared from immune sera either by precipitation with ammonium sulfate or by purification on immobilized Protein A (Pharmacia LKB Biotechnology, Piscataway, N.J.). Likewise, monoclonal antibodies are prepared from mouse ascites fluid by ammonium sulfate precipitation or chromatography on immobilized Protein A. Partially purified immunoglobulin is covalently attached to a chromatographic resin such as CnBr-activated SEPHAROSE™ (Pharmacia LKB Biotechnology). The antibody is coupled to the resin, the resin is blocked, and the derivative resin is washed according to the manufacturer's 10 instructions.

15 Such an immunoaffinity column is utilized in the purification of PRO polypeptide by preparing a fraction from cells containing PRO polypeptide in a soluble form. This preparation is derived by solubilization of the whole cell or of a subcellular fraction obtained via differential centrifugation by the addition of detergent or by other methods well known in the art. Alternatively, soluble PRO polypeptide containing a signal sequence may be secreted in useful quantity into the medium in which the cells are grown.

20 A soluble PRO polypeptide-containing preparation is passed over the immunoaffinity column, and the column is washed under conditions that allow the preferential absorbance of PRO polypeptide (e.g., high ionic strength buffers in the presence of detergent). Then, the column is eluted under conditions that disrupt antibody/PRO polypeptide binding (e.g., a low pH buffer such as approximately pH 2-3, or a high concentration of a chaotrope such as urea or thiocyanate ion), and PRO polypeptide is collected.

EXAMPLE 146: Drug Screening

25 This invention is particularly useful for screening compounds by using PRO polypeptides or binding fragment thereof in any of a variety of drug screening techniques. The PRO polypeptide or fragment employed in such a test may either be free in solution, affixed to a solid support, borne on a cell surface, or located intracellularly. One method of drug screening utilizes eukaryotic or prokaryotic host cells which are stably transformed with recombinant nucleic acids expressing the PRO polypeptide or fragment. Drugs are screened 30 against such transformed cells in competitive binding assays. Such cells, either in viable or fixed form, can be used for standard binding assays. One may measure, for example, the formation of complexes between PRO polypeptide or a fragment and the agent being tested. Alternatively, one can examine the diminution in complex formation between the PRO polypeptide and its target cell or target receptors caused by the agent being tested.

35 Thus, the present invention provides methods of screening for drugs or any other agents which can affect a PRO polypeptide-associated disease or disorder. These methods comprise contacting such an agent with an PRO polypeptide or fragment thereof and assaying (i) for the presence of a complex between the agent and the PRO polypeptide or fragment, or (ii) for the presence of a complex between the PRO polypeptide or fragment and the cell, by methods well known in the art. In such competitive binding assays, the PRO polypeptide or fragment is typically labeled. After suitable incubation, free PRO polypeptide or fragment is

separated from that present in bound form, and the amount of free or uncomplexed label is a measure of the ability of the particular agent to bind to PRO polypeptide or to interfere with the PRO polypeptide/cell complex.

Another technique for drug screening provides high throughput screening for compounds having suitable binding affinity to a polypeptide and is described in detail in WO 84/03564, published on September 5 13, 1984. Briefly stated, large numbers of different small peptide test compounds are synthesized on a solid substrate, such as plastic pins or some other surface. As applied to a PRO polypeptide, the peptide test compounds are reacted with PRO polypeptide and washed. Bound PRO polypeptide is detected by methods well known in the art. Purified PRO polypeptide can also be coated directly onto plates for use in the aforementioned drug screening techniques. In addition, non-neutralizing antibodies can be used to capture the 10 peptide and immobilize it on the solid support.

This invention also contemplates the use of competitive drug screening assays in which neutralizing antibodies capable of binding PRO polypeptide specifically compete with a test compound for binding to PRO polypeptide or fragments thereof. In this manner, the antibodies can be used to detect the presence of any peptide which shares one or more antigenic determinants with PRO polypeptide.

15

EXAMPLE 147: Rational Drug Design

The goal of rational drug design is to produce structural analogs of biologically active polypeptide of interest (*i.e.*, a PRO polypeptide) or of small molecules with which they interact, *e.g.*, agonists, antagonists, or inhibitors. Any of these examples can be used to fashion drugs which are more active or stable forms of 20 the PRO polypeptide or which enhance or interfere with the function of the PRO polypeptide *in vivo* (*c.f.*, Hodgson, Bio/Technology, 9: 19-21 (1991)).

In one approach, the three-dimensional structure of the PRO polypeptide, or of an PRO polypeptide-inhibitor complex, is determined by x-ray crystallography, by computer modeling or, most typically, by a combination of the two approaches. Both the shape and charges of the PRO polypeptide must 25 be ascertained to elucidate the structure and to determine active site(s) of the molecule. Less often, useful information regarding the structure of the PRO polypeptide may be gained by modeling based on the structure of homologous proteins. In both cases, relevant structural information is used to design analogous PRO polypeptide-like molecules or to identify efficient inhibitors. Useful examples of rational drug design may include molecules which have improved activity or stability as shown by Braxton and Wells, Biochemistry, 30 31:7796-7801 (1992) or which act as inhibitors, agonists, or antagonists of native peptides as shown by Athauda *et al.*, J. Biochem., 113:742-746 (1993).

It is also possible to isolate a target-specific antibody, selected by functional assay, as described above, and then to solve its crystal structure. This approach, in principle, yields a pharmacore upon which subsequent drug design can be based. It is possible to bypass protein crystallography altogether by generating 35 anti-idiotypic antibodies (anti-ids) to a functional, pharmacologically active antibody. As a mirror image of a mirror image, the binding site of the anti-ids would be expected to be an analog of the original receptor. The anti-id could then be used to identify and isolate peptides from banks of chemically or biologically produced

peptides. The isolated peptides would then act as the pharmacore.

By virtue of the present invention, sufficient amounts of the PRO polypeptide may be made available to perform such analytical studies as X-ray crystallography. In addition, knowledge of the PRO polypeptide amino acid sequence provided herein will provide guidance to those employing computer modeling techniques in place of or in addition to x-ray crystallography.

5

EXAMPLE 148: Stimulation of Heart Neonatal Hypertrophy (Assay 1)

This assay is designed to measure the ability of PRO polypeptides to stimulate hypertrophy of neonatal heart. PRO polypeptides testing positive in this assay are expected to be useful for the therapeutic treatment of various cardiac insufficiency disorders.

10

Cardiac myocytes from 1-day old Harlan Sprague Dawley rats were obtained. Cells (180 μ l at 7.5 \times 10⁴/ml, serum <0.1%, freshly isolated) are added on day 1 to 96-well plates previously coated with DMEM/F12 + 4% FCS. Test samples containing the test PRO polypeptide or growth medium only (negative control) (20 μ l/well) are added directly to the wells on day 1. PGF (20 μ l/well) is then added on day 2 at final concentration of 10⁻⁶ M. The cells are then stained on day 4 and visually scored on day 5, wherein cells showing no increase in size as compared to negative controls are scored 0.0, cells showing a small to moderate increase in size as compared to negative controls are scored 1.0 and cells showing a large increase in size as compared to negative controls are scored 2.0. A positive result in the assay is a score of 1.0 or greater.

15

The following polypeptides tested positive in this assay: PRO1312.

20

EXAMPLE 149: Stimulation of Endothelial Cell Proliferation (Assay 8)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to stimulate adrenal cortical capillary endothelial cell (ACE) growth. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

25

Bovine adrenal cortical capillary endothelial (ACE) cells (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus VEGF (5 ng/ml); and (4) ACE cells plus FGF (5ng/ml). The control or test sample, (in 100 microliter volumes), was then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO₂. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

The activity of a PRO polypeptide was calculated as the fold increase in proliferation (as determined by the acid phosphatase activity, OD 405 nm) relative to (1) cell only background, and (2) relative to maximum stimulation by VEGF. VEGF (at 3-10 ng/ml) and FGF (at 1-5 ng/ml) were employed as an activity reference for maximum stimulation. Results of the assay were considered "positive" if the observed stimulation was \geq 50% increase over background. VEGF (5 ng/ml) control at 1% dilution gave 1.24 fold stimulation; FGF (5 ng/ml) control at 1% dilution gave 1.46 fold stimulation.

5

The following PRO polypeptides tested positive in this assay: PRO1154 and PRO1186.

EXAMPLE 150: Inhibition of Vascular Endothelial Growth Factor (VEGF) Stimulated Proliferation of Endothelial Cell Growth (Assay 9)

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The ability of various PRO polypeptides to inhibit VEGF stimulated proliferation of endothelial cells was tested. Polypeptides testing positive in this assay are useful for inhibiting endothelial cell growth in mammals where such an effect would be beneficial, e.g., for inhibiting tumor growth.

15

Specifically, bovine adrenal cortical capillary endothelial cells (ACE) (from primary culture, maximum of 12-14 passages) were plated in 96-well plates at 500 cells/well per 100 microliter. Assay media included low glucose DMEM, 10% calf serum, 2 mM glutamine, and 1X penicillin/streptomycin/fungizone. Control wells included the following: (1) no ACE cells added; (2) ACE cells alone; (3) ACE cells plus 5 ng/ml FGF; (4) ACE cells plus 3 ng/ml VEGF; (5) ACE cells plus 3 ng/ml VEGF plus 1 ng/ml TGF-beta; and (6) ACE cells plus 3 ng/ml VEGF plus 5 ng/ml LIF. The test samples, poly-his tagged PRO polypeptides (in 100 microliter volumes), were then added to the wells (at dilutions of 1%, 0.1% and 0.01%, respectively). The cell cultures were incubated for 6-7 days at 37°C/5% CO₂. After the incubation, the media in the wells was aspirated, and the cells were washed 1X with PBS. An acid phosphatase reaction mixture (100 microliter; 0.1M sodium acetate, pH 5.5, 0.1% Triton X-100, 10 mM p-nitrophenyl phosphate) was then added to each well. After a 2 hour incubation at 37°C, the reaction was stopped by addition of 10 microliters 1N NaOH. Optical density (OD) was measured on a microplate reader at 405 nm.

20

25 The activity of PRO polypeptides was calculated as the percent inhibition of VEGF (3 ng/ml) stimulated proliferation (as determined by measuring acid phosphatase activity at OD 405 nm) relative to the cells without stimulation. TGF-beta was employed as an activity reference at 1 ng/ml, since TGF-beta blocks 70-90% of VEGF-stimulated ACE cell proliferation. The results are indicative of the utility of the PRO polypeptides in cancer therapy and specifically in inhibiting tumor angiogenesis. Numerical values (relative inhibition) are determined by calculating the percent inhibition of VEGF stimulated proliferation by the PRO polypeptides relative to cells without stimulation and then dividing that percentage into the percent inhibition obtained by TGF- β at 1 ng/ml which is known to block 70-90% of VEGF stimulated cell proliferation. The results are considered positive if the PRO polypeptide exhibits 30% or greater inhibition of VEGF stimulation of endothelial cell growth (relative inhibition 30% or greater).

30

35 The following polypeptide tested positive in this assay: PRO812.

EXAMPLE 151: Stimulatory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 24)

This example shows that certain polypeptides of the invention are active as a stimulator of the proliferation of stimulated T-lymphocytes. Compounds which stimulate proliferation of lymphocytes are useful therapeutically where enhancement of an immune response is beneficial. A therapeutic agent may take the form of antagonists of the polypeptide of the invention, for example, murine-human chimeric, humanized or human antibodies against the polypeptide.

5 The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from 10 mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO₂) and then washed and resuspended to 3x10⁶ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The 15 stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

The assay is prepared by plating in triplicate wells a mixture of:

100:1 of test sample diluted to 1% or to 0.1%,

50 :1 of irradiated stimulator cells, and

50 :1 of responder PBMC cells.

20 100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO₂ for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mCi/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% 25 penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknica), centrifuging at 2000 rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1x10⁷ cells/ml of assay media. The assay is then conducted as described above.

30 Positive increases over control are considered positive with increases of greater than or equal to 180% being preferred. However, any value greater than control indicates a stimulatory effect for the test protein.

The following PRO polypeptides tested positive in this assay: PRO826, PRO1068, PRO1184, PRO1346 and PRO1375.

EXAMPLE 152: Retinal Neuron Survival (Assay 52)

35 This example demonstrates that certain PRO polypeptides have efficacy in enhancing the survival of retinal neuron cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosum, AMD, etc.

Sprague Dawley rat pups at postnatal day 7 (mixed population: glia and retinal neuronal types) are killed by decapitation following CO₂ anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca²⁺, Mg²⁺-free PBS. The retinas are incubated at 37°C for 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated 5 at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N2 and with or without the specific test PRO polypeptide. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO₂. After 2-3 days in culture, cells are stained with calcein AM then fixed using 4% paraformaldehyde and stained with DAPI for determination of total cell count. The total cells (fluorescent) are quantified at 20X objective magnification using CCD camera and NIH image software for MacIntosh.

10 Fields in the well are chosen at random.

The effect of various concentration of PRO polypeptides are reported herein where percent survival is calculated by dividing the total number of calcein AM positive cells at 2-3 days in culture by the total number of DAPI-labeled cells at 2-3 days in culture. Anything above 30% survival is considered positive.

15 The following PRO polypeptides tested positive in this assay using polypeptide concentrations within the range of 0.01% to 1.0% in the assay: PRO828, PRO826, PRO1068 and PRO1132.

EXAMPLE 153: Rod Photoreceptor Cell Survival (Assay 56)

20 This assay shows that certain polypeptides of the invention act to enhance the survival/proliferation of rod photoreceptor cells and, therefore, are useful for the therapeutic treatment of retinal disorders or injuries including, for example, treating sight loss in mammals due to retinitis pigmentosum, AMD, etc.

Sprague Dawley rat pups at 7 day postnatal (mixed population: glia and retinal neuronal cell types) are killed by decapitation following CO₂ anesthesia and the eyes are removed under sterile conditions. The neural retina is dissected away from the pigment epithelium and other ocular tissue and then dissociated into a single cell suspension using 0.25% trypsin in Ca²⁺, Mg²⁺-free PBS. The retinas are incubated at 37°C for 25 7-10 minutes after which the trypsin is inactivated by adding 1 ml soybean trypsin inhibitor. The cells are plated at 100,000 cells per well in 96 well plates in DMEM/F12 supplemented with N₂. Cells for all experiments are grown at 37°C in a water saturated atmosphere of 5% CO₂. After 2-3 days in culture, cells are fixed using 4% paraformaldehyde, and then stained using CellTracker Green CMFDA. Rho 4D2 (ascites or IgG 1:100), a monoclonal antibody directed towards the visual pigment rhodopsin is used to detect rod 30 photoreceptor cells by indirect immunofluorescence. The results are calculated as % survival: total number of calcein- rhodopsin positive cells at 2-3 days in culture, divided by the total number of rhodopsin positive cells at time 2-3 days in culture. The total cells (fluorescent) are quantified at 20x objective magnification using a CCD camera and NIH image software for MacIntosh. Fields in the well are chosen at random.

35 The following polypeptides tested positive in this assay: PRO536, PRO943, PRO828, PRO826, PRO1068 and PRO1132.

EXAMPLE 154: Induction of c-fos in Endothelial Cells (Assay 34)

This assay is designed to determine whether PRO polypeptides show the ability to induce c-fos in endothelial cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of conditions or disorders where angiogenesis would be beneficial including, for example, wound healing, and the like (as would agonists of these PRO polypeptides). Antagonists of the PRO 5 polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of cancerous tumors.

Human venous umbilical vein endothelial cells (HUVEC, Cell Systems) in growth media (50% Ham's F12 w/o GHT: low glucose, and 50% DMEM without glycine: with NaHCO₃, 1% glutamine, 10 mM HEPES, 10% FBS, 10 ng/ml bFGF) were plated on 96-well microtiter plates at a cell density of 1x10⁴ 10 cells/well. The day after plating, the cells were starved by removing the growth media and treating the cells with 100 μ l/well test samples and controls (positive control = growth media; negative control = Protein 32 buffer = 10 mM HEPES, 140 mM NaCl, 4% (w/v) mannitol, pH 6.8). The cells were incubated for 30 minutes at 37°C, in 5% CO₂. The samples were removed, and the first part of the bDNA kit protocol (Chiron Diagnostics, cat. #6005-037) was followed, where each capitalized reagent/buffer listed below was available 15 from the kit.

Briefly, the amounts of the TM Lysis Buffer and Probes needed for the tests were calculated based 20 on information provided by the manufacturer. The appropriate amounts of thawed Probes were added to the TM Lysis Buffer. The Capture Hybridization Buffer was warmed to room temperature. The bDNA strips were set up in the metal strip holders, and 100 μ l of Capture Hybridization Buffer was added to each b-DNA 25 well needed, followed by incubation for at least 30 minutes. The test plates with the cells were removed from the incubator, and the media was gently removed using the vacuum manifold. 100 μ l of Lysis Hybridization Buffer with Probes were quickly pipetted into each well of the microtiter plates. The plates were then incubated at 55°C for 15 minutes. Upon removal from the incubator, the plates were placed on the vortex mixer with the microtiter adapter head and vortexed on the #2 setting for one minute. 80 μ l of the lysate was removed and added to the bDNA wells containing the Capture Hybridization Buffer, and pipetted up and down to mix. The plates were incubated at 53°C for at least 16 hours.

On the next day, the second part of the bDNA kit protocol was followed. Specifically, the plates 30 were removed from the incubator and placed on the bench to cool for 10 minutes. The volumes of additions needed were calculated based upon information provided by the manufacturer. An Amplifier Working Solution was prepared by making a 1:100 dilution of the Amplifier Concentrate (20 fm/ μ l) in AL Hybridization Buffer. The hybridization mixture was removed from the plates and washed twice with Wash A. 50 μ l of Amplifier 35 Working Solution was added to each well and the wells were incubated at 53°C for 30 minutes. The plates were then removed from the incubator and allowed to cool for 10 minutes. The Label Probe Working Solution was prepared by making a 1:100 dilution of Label Concentrate (40 pmoles/ μ l) in AL Hybridization Buffer. After the 10-minute cool-down period, the amplifier hybridization mixture was removed and the plates were washed twice with Wash A. 50 μ l of Label Probe Working Solution was added to each well and the wells were incubated at 53°C for 15 minutes. After cooling for 10 minutes, the Substrate was warmed to room

temperature. Upon addition of 3 μ l of Substrate Enhancer to each ml of Substrate needed for the assay, the plates were allowed to cool for 10 minutes, the label hybridization mixture was removed, and the plates were washed twice with Wash A and three times with Wash D. 50 μ l of the Substrate Solution with Enhancer was added to each well. The plates were incubated for 30 minutes at 37°C and RLU was read in an appropriate luminometer.

5 The replicates were averaged and the coefficient of variation was determined. The measure of activity of the fold increase over the negative control (Protein 32/HEPES buffer described above) value was indicated by chemiluminescence units (RLU). The results are considered positive if the PRO polypeptide exhibits at least a two-fold value over the negative buffer control. Negative control = 1.00 RLU at 1.00% dilution. Positive control = 8.39 RLU at 1.00% dilution.

10 The following PRO polypeptides tested positive in this assay: PRO535, PRO826, PRO819, PRO1126, PRO1160 and PRO1387.

EXAMPLE 155: Inhibitory Activity in Mixed Lymphocyte Reaction (MLR) Assay (Assay 67)

15 This example shows that one or more of the polypeptides of the invention are active as inhibitors of the proliferation of stimulated T-lymphocytes. Compounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial.

The basic protocol for this assay is described in Current Protocols in Immunology, unit 3.12; edited by J E Coligan, A M Kruisbeek, D H Marglies, E M Shevach, W Strober, National Institutes of Health, Published by John Wiley & Sons, Inc.

20 More specifically, in one assay variant, peripheral blood mononuclear cells (PBMC) are isolated from mammalian individuals, for example a human volunteer, by leukopheresis (one donor will supply stimulator PBMCs, the other donor will supply responder PBMCs). If desired, the cells are frozen in fetal bovine serum and DMSO after isolation. Frozen cells may be thawed overnight in assay media (37°C, 5% CO₂) and then washed and resuspended to 3x10⁶ cells/ml of assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate). The stimulator PBMCs are prepared by irradiating the cells (about 3000 Rads).

25 The assay is prepared by plating in triplicate wells a mixture of:
100:1 of test sample diluted to 1% or to 0.1%,
50 :1 of irradiated stimulator cells, and
30 :1 of responder PBMC cells.

100 microliters of cell culture media or 100 microliter of CD4-IgG is used as the control. The wells are then incubated at 37°C, 5% CO₂ for 4 days. On day 5, each well is pulsed with tritiated thymidine (1.0 mC/well; Amersham). After 6 hours the cells are washed 3 times and then the uptake of the label is evaluated.

35 In another variant of this assay, PBMCs are isolated from the spleens of Balb/c mice and C57B6 mice. The cells are teased from freshly harvested spleens in assay media (RPMI; 10% fetal bovine serum, 1% penicillin/streptomycin, 1% glutamine, 1% HEPES, 1% non-essential amino acids, 1% pyruvate) and the PBMCs are isolated by overlaying these cells over Lympholyte M (Organon Teknika), centrifuging at 2000

rpm for 20 minutes, collecting and washing the mononuclear cell layer in assay media and resuspending the cells to 1×10^7 cells/ml of assay media. The assay is then conducted as described above.

Any decreases below control is considered to be a positive result for an inhibitory compound, with decreases of less than or equal to 80% being preferred. However, any value less than control indicates an inhibitory effect for the test protein.

5 The following polypeptide tested positive in this assay: PRO1114, PRO836, PRO1159, PRO1312, PRO1192, PRO1195 and PRO1387.

EXAMPLE 156: Mouse Kidney Mesangial Cell Proliferation Assay (Assay 92)

This assay shows that certain polypeptides of the invention act to induce proliferation of mammalian 10 kidney mesangial cells and, therefore, are useful for treating kidney disorders associated with decreased mesangial cell function such as Berger disease or other nephropathies associated with Schönlein-Henoch purpura,

celiac disease, dermatitis herpetiformis or Crohn disease. The assay is performed as follows. On day one, 15 mouse kidney mesangial cells are plated on a 96 well plate in growth media (3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95% fetal bovine serum, 5% supplemented with 14 mM HEPES) and grown overnight. On day 2, PRO polypeptides are diluted at 2 concentrations (1% and 0.1%) in serum-free medium and added to the cells. Control samples are serum-free medium alone. On day 4, 20 μ l of the Cell Titer 96 Aqueous one solution reagent (Progema) was added to each well and the colorimetric reaction was allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive 20 in the assay is anything that gives an absorbance reading which is at least 15% above the control reading.

The following polypeptide tested positive in this assay: PRO819, PRO813 and PRO1066.

EXAMPLE 157: Pericyte c-Fos Induction (Assay 93)

This assay shows that certain polypeptides of the invention act to induce the expression of c-fos in 25 pericyte cells and, therefore, are useful not only as diagnostic markers for particular types of pericyte-associated tumors but also for giving rise to antagonists which would be expected to be useful for the therapeutic treatment of pericyte-associated tumors. Specifically, on day 1, pericytes are received from VEC Technologies and all but 5 ml of media is removed from flask. On day 2, the pericytes are trypsinized, 30 washed, spun and then plated onto 96 well plates. On day 7, the media is removed and the pericytes are treated with 100 μ l of PRO polypeptide test samples and controls (positive control = DME + 5% serum +/- PDGF at 500 ng/ml; negative control = protein 32). Replicates are averaged and SD/CV are determined. Fold increase over Protein 32 (buffer control) value indicated by chemiluminescence units (RLU) luminometer reading versus frequency is plotted on a histogram. Two-fold above Protein 32 value is considered positive for the assay. ASY Matrix: Growth media = low glucose DMEM = 20% FBS + 1X pen strep + 1X fungizone. 35 Assay Media = low glucose DMEM + 5% FBS.

The following polypeptides tested positive in this assay: PRO943 and PRO819.

EXAMPLE 158: Detection of PRO Polypeptides That Affect Glucose or FFA Uptake by Primary Rat Adipocytes (Assay 94)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by adipocyte cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by adipocytes would be beneficial including, for example, obesity, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat adipocytes, and allowed to incubate overnight. Samples are taken at 4 and 16 hours and assayed for glycerol, glucose and FFA uptake. After the 16 hour incubation, insulin is added to the media and allowed to incubate for 4 hours. At this time, a sample is taken and glycerol, glucose and FFA uptake is measured. Media containing insulin without the PRO polypeptide is used as a positive reference control. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as stimulators of glucose and/or FFA uptake in this assay: PRO1114, PRO1007, PRO1066, PRO848, PRO1182, PRO1198, PRO1192, PRO1271, PRO1375 and PRO1387.

The following PRO polypeptides tested positive as inhibitors of glucose and/or FFA uptake in this assay: PRO1184, PRO1360, PRO1309, PRO1154, PRO1181, PRO1186, PRO1160 and PRO1384.

EXAMPLE 159: Chondrocyte Re-differentiation Assay (Assay 110)

This assay shows that certain polypeptides of the invention act to induce redifferentiation of chondrocytes, therefore, are expected to be useful for the treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis. The assay is performed as follows. Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of metacarpophalangeal joints of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm² in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are then seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of the test PRO polypeptide, 5 nM staurosporin (positive control) or medium alone (negative control) is added to give a final volume of 200 µl/well. After 5 days of incubation at 37°C, a picture of each well is taken and the differentiation state of the chondrocytes is determined. A positive result in the assay occurs when the redifferentiation of the chondrocytes is determined to be more similar to the positive control than the negative control.

The following polypeptide tested positive in this assay: PRO1282, PRO1310, PRO619, PRO943, PRO820, PRO1080, PRO1016, PRO1007, PRO1056, PRO791, PRO1111, PRO1184, PRO1360, PRO1309, PRO1107, PRO1132, PRO1131, PRO848, PRO1181, PRO1186, PRO1159, PRO1312, PRO1192 and PRO1384.

EXAMPLE 160: Chondrocyte Proliferation Assay (Assay 111)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to induce the proliferation and/or redifferentiation of chondrocytes in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of various bone and/or cartilage disorders such as, for example, sports injuries and arthritis.

5 Porcine chondrocytes are isolated by overnight collagenase digestion of articular cartilage of the metacarpophalangeal joint of 4-6 month old female pigs. The isolated cells are then seeded at 25,000 cells/cm² in Ham F-12 containing 10% FBS and 4 µg/ml gentamycin. The culture media is changed every third day and the cells are reseeded to 25,000 cells/cm² every five days. On day 12, the cells are seeded in 96 well plates at 5,000 cells/well in 100 µl of the same media without serum and 100 µl of either serum-free medium (negative 10 control), staurosporin (final concentration of 5 nM; positive control) or the test PRO polypeptide are added to give a final volume of 200 µl/well. After 5 days at 37°C, 20 µl of Alamar blue is added to each well and the plates are incubated for an additional 3 hours at 37°C. The fluorescence is then measured in each well (Ex:530 nm; Em: 590 nm). The fluorescence of a plate containing 200 µl of the serum-free medium is measured to obtain the background. A positive result in the assay is obtained when the fluorescence of the 15 PRO polypeptide treated sample is more like that of the positive control than the negative control.

The following PRO polypeptides tested positive in this assay: PRO1310, PRO844, PRO1312, PRO1192 and PRO1387.

EXAMPLE 161: Induction of Pancreatic β-Cell Precursor Proliferation (Assay 117)

20 This assay shows that certain polypeptides of the invention act to induce an increase in the number of pancreatic β-cell precursor cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative 25 PCR (RTQ-PCR); wherein the marker being evaluated is a transcription factor called Pdx1.

The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with 30 laminin, 20 µg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression 35 of the relevant β-cell marker as compared to untreated controls.

14F/1640 is RPMI1640 (Gibco) plus the following:

group A 1:1000

group B 1:1000

recombinant human insulin 10 μ g/ml

Aprotinin (50 μ g/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60 μ g/ml

5 Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

Epidermal Growth Factor, 100 μ g (BRL 100004)

Triiodothyronine, 10 μ l of 5 \times 10⁻⁶ M (Sigma T5516)

10 Ethanolamine, 100 μ l of 10⁻¹ M (Sigma E0135)

Phosphoethalamine, 100 μ l of 10⁻¹ M (Sigma P0503)

Selenium, 4 μ l of 10⁻¹ M (Aesar #12574)

Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2 μ l of 5 \times 10⁻³ M (Sigma #H0135)

15 Progesterone, 100 μ l of 1 \times 10⁻³ M (Sigma #P6149)

Forskolin, 500 μ l of 20mM (Calbiochem #344270)

Minimal media:

RPMI 1640 plus transferrin (10 μ g/ml), insulin (1 μ g/ml), gentamycin (100 ng/ml), aprotinin (50 μ g/ml) and BPE (15 μ g/ml).

20 Defined media:

RPMI 1640 plus transferrin (10 μ g/ml), insulin (1 μ g/ml), gentamycin (100 ng/ml) and aprotinin (50 μ g/ml).

The following polypeptides tested positive in this assay: PRO1310, PRO1188, PRO1131 and PRO1387.

25

EXAMPLE 162: Detection of Polypeptides That Affect Glucose or FFA Uptake in Skeletal Muscle (Assay 106)

This assay is designed to determine whether PRO polypeptides show the ability to affect glucose or FFA uptake by skeletal muscle cells. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of disorders where either the stimulation or inhibition of glucose uptake by skeletal muscle would be beneficial including, for example, diabetes or hyper- or hypo-insulinemia.

In a 96 well format, PRO polypeptides to be assayed are added to primary rat differentiated skeletal muscle, and allowed to incubate overnight. Then fresh media with the PRO polypeptide and +/- insulin are added to the wells. The sample media is then monitored to determine glucose and FFA uptake by the skeletal muscle cells. The insulin will stimulate glucose and FFA uptake by the skeletal muscle, and insulin in media without the PRO polypeptide is used as a positive control, and a limit for scoring. As the PRO polypeptide being tested may either stimulate or inhibit glucose and FFA uptake, results are scored as positive in the assay

if greater than 1.5 times or less than 0.5 times the insulin control.

The following PRO polypeptides tested positive as either stimulators or inhibitors of glucose and/or FFA uptake in this assay: PRO358, PRO1016, PRO1007, PRO826, PRO1066, PRO1029 and PRO1309.

EXAMPLE 163: Fetal Hemoglobin Induction in an Erythroblastic Cell Line (Assay 107)

5 This assay is useful for screening PRO polypeptides for the ability to induce the switch from adult hemoglobin to fetal hemoglobin in an erythroblastic cell line. Molecules testing positive in this assay are expected to be useful for therapeutically treating various mammalian hemoglobin-associated disorders such as the various thalassemias. The assay is performed as follows. Erythroblastic cells are plated in standard growth medium at 1000 cells/well in a 96 well format. PRO polypeptides are added to the growth medium at a 10 concentration of 0.2% or 2% and the cells are incubated for 5 days at 37°C. As a positive control, cells are treated with 100μM hemin and as a negative control, the cells are untreated. After 5 days, cell lysates are prepared and analyzed for the expression of gamma globin (a fetal marker). A positive in the assay is a gamma globin level at least 2-fold above the negative control.

15 The following polypeptides tested positive in this assay: PRO1114, PRO826, PRO1066, PRO844, PRO1192 and PRO1358.

EXAMPLE 164: Induction of Pancreatic β-Cell Precursor Differentiation (Assay 89)

20 This assay shows that certain polypeptides of the invention act to induce differentiation of pancreatic β-cell precursor cells into mature pancreatic β-cells and, therefore, are useful for treating various insulin deficient states in mammals, including diabetes mellitus. The assay is performed as follows. The assay uses a primary culture of mouse fetal pancreatic cells and the primary readout is an alteration in the expression of markers that represent either β-cell precursors or mature β-cells. Marker expression is measured by real time quantitative PCR (RTQ-PCR); wherein the marker being evaluated is insulin.

25 The pancreata are dissected from E14 embryos (CD1 mice). The pancreata are then digested with collagenase/dispase in F12/DMEM at 37°C for 40 to 60 minutes (collagenase/dispase, 1.37 mg/ml, Boehringer Mannheim, #1097113). The digestion is then neutralized with an equal volume of 5% BSA and the cells are washed once with RPMI1640. At day 1, the cells are seeded into 12-well tissue culture plates (pre-coated with laminin, 20μg/ml in PBS, Boehringer Mannheim, #124317). Cells from pancreata from 1-2 embryos are distributed per well. The culture medium for this primary culture is 14F/1640. At day 2, the media is removed 30 and the attached cells washed with RPMI/1640. Two mls of minimal media are added in addition to the protein to be tested. At day 4, the media is removed and RNA prepared from the cells and marker expression analyzed by real time quantitative RT-PCR. A protein is considered to be active in the assay if it increases the expression of the relevant β-cell marker as compared to untreated controls.

14F/1640 is RPMI1640 (Gibco) plus the following:

35 group A 1:1000
group B 1:1000
recombinant human insulin 10 μg/ml

Aprotinin (50 μ g/ml) 1:2000 (Boehringer manheim #981532)

Bovine pituitary extract (BPE) 60 μ g/ml

Gentamycin 100 ng/ml

Group A : (in 10ml PBS)

Transferrin, 100mg (Sigma T2252)

5 Epidermal Growth Factor, 100 μ g (BRL 100004)
Triiodothyronine, 10 μ l of 5 \times 10⁻⁶ M (Sigma T5516)
Ethanolamine, 100 μ l of 10⁻¹ M (Sigma E0135)
Phosphoethalamine, 100 μ l of 10⁻¹ M (Sigma P0503)
Selenium, 4 μ l of 10⁻¹ M (Aesar #12574)

10 Group C : (in 10ml 100% ethanol)

Hydrocortisone, 2 μ l of 5 \times 10⁻³ M (Sigma #H0135)
Progesterone, 100 μ l of 1 \times 10⁻³ M (Sigma #P6149)
Forskolin, 500 μ l of 20mM (Calbiochem #344270)

Minimal media:

15 RPMI 1640 plus transferrin (10 μ g/ml), insulin (1 μ g/ml), gentamycin (100 ng/ml), aprotinin (50 μ g/ml) and BPE (15 μ g/ml).

Defined media:

RPMI 1640 plus transferrin (10 μ g/ml), insulin (1 μ g/ml), gentamycin (100 ng/ml) and aprotinin (50 μ g/ml).

20 The following polypeptides were positive in this assay: PRO1188, PRO1132, PRO1131 and PRO1181.

EXAMPLE 165: Skin Vascular Permeability Assay (Assay 64)

This assay shows that certain polypeptides of the invention stimulate an immune response and induce inflammation by inducing mononuclear cell, eosinophil and PMN infiltration at the site of injection of the animal. Compounds which stimulate an immune response are useful therapeutically where stimulation of an immune response is beneficial. This skin vascular permeability assay is conducted as follows. Hairless guinea pigs weighing 350 grams or more are anesthetized with ketamine (75-80 mg/Kg) and 5 mg/Kg xylazine intramuscularly (IM). A sample of purified polypeptide of the invention or a conditioned media test sample is injected intradermally onto the backs of the test animals with 100 μ l per injection site. It is possible to have about 10-30, preferably about 16-24, injection sites per animal. One μ l of Evans blue dye (1% in physiologic buffered saline) is injected intracardially. Blemishes at the injection sites are then measured (mm diameter) at 1 hr and 6 hr post injection. Animals were sacrificed at 6 hrs after injection. Each skin injection site is biopsied and fixed in formalin. The skins are then prepared for histopathologic evaluation. Each site is evaluated for inflammatory cell infiltration into the skin. Sites with visible inflammatory cell inflammation are scored as positive. Inflammatory cells may be neutrophilic, eosinophilic, monocytic or lymphocytic. At least a minimal perivascular infiltrate at the injection site is scored as positive, no infiltrate at the site of injection is

scored as negative.

The following polypeptide tested positive in this assay: PRO1007, PRO1358 and PRO1375.

EXAMPLE 166: Induction of Endothelial Cell Apoptosis (ELISA) (Assay 109)

The ability of PRO polypeptides to induce apoptosis in endothelial cells was tested in human venous
5 umbilical vein endothelial cells (HUVEC, Cell Systems) using a 96-well format, in 0% serum media
supplemented with 100 ng/ml VEGF, 0.1% BSA, 1X penn/strep. A positive result in this assay indicates the
usefulness of the polypeptide for therapeutically treating any of a variety of conditions associated with
undesired endothelial cell growth including, for example, the inhibition of tumor growth. The 96-well plates
used were manufactured by Falcon (No. 3072). Coating of 96 well plates were prepared by allowing
10 gelatinization to occur for >30 minutes with 100 μ l of 0.2% gelatin in PBS solution. The gelatin mix was
aspirated thoroughly before plating HUVEC cells at a final concentration of 2×10^4 cells/ml in 10% serum
containing medium - 100 μ l volume per well. The cells were grown for 24 hours before adding test samples
containing the PRO polypeptide of interest.

15 To all wells, 100 μ l of 0% serum media (Cell Systems) complemented with 100 ng/ml VEGF, 0.1%
BSA, 1X penn/strep was added. Test samples containing PRO polypeptides were added in triplicate at
dilutions of 1%, 0.33% and 0.11%. Wells without cells were used as a blank and wells with cells only were
used as a negative control. As a positive control, 1:3 serial dilutions of 50 μ l of a 3x stock of staurosporine
were used. The cells were incubated for 24 to 35 hours prior to ELISA.

20 ELISA was used to determine levels of apoptosis preparing solutions according to the Boehringer
Manual [Boehringer, Cell Death Detection ELISA plus, Cat No. 1 920 685]. Sample preparations: 96 well
plates were spun down at 1 krpm for 10 minutes (200g); the supernatant was removed by fast inversion,
placing the plate upside down on a paper towel to remove residual liquid. To each well, 200 μ l of 1X Lysis
buffer was added and incubation allowed at room temperature for 30 minutes without shaking. The plates were
25 spun down for 10 minutes at 1 krpm, and 20 μ l of the lysate (cytoplasmic fraction) was transferred into
streptavidin coated MTP. 80 μ l of immunoreagent mix was added to the 20 μ l lysate in each well. The MTP
was covered with adhesive foil and incubated at room temperature for 2 hours by placing it on an orbital
shaker (200 rpm). After two hours, the supernatant was removed by suction and the wells rinsed three times
30 with 250 μ l of 1X incubation buffer per well (removed by suction). Substrate solution was added (100 μ l) into
each well and incubated on an orbital shaker at room temperature at 250 rpm until color development was
sufficient for a photometric analysis (approx. after 10-20 minutes). A 96 well reader was used to read the
plates at 405 nm, reference wavelength, 492 nm. The levels obtained for PIN 32 (control buffer) was set to
100%. Samples with levels > 130% were considered positive for induction of apoptosis.

The following PRO polypeptides tested positive in this assay: PRO844.

35 **EXAMPLE 167: Guinea Pig Vascular Leak (Assay 32)**

This assay is designed to determine whether PRO polypeptides of the present invention show the
ability to induce vascular permeability. Polypeptides testing positive in this assay are expected to be useful

for the therapeutic treatment of conditions which would benefit from enhanced vascular permeability including, for example, conditions which may benefit from enhanced local immune system cell infiltration.

Hairless guinea pigs weighing 350 grams or more were anesthetized with Ketamine (75-80 mg/kg) and 5 mg/kg Xylazine intramuscularly. Test samples containing the PRO polypeptide or a physiological buffer without the test polypeptide are injected into skin on the back of the test animals with 100 μ l per injection site 5 intradermally. There were approximately 16-24 injection sites per animal. One ml of Evans blue dye (1% in PBS) is then injected intracardially. Skin vascular permeability responses to the compounds (*i.e.*, blemishes at the injection sites of injection) are visually scored by measuring the diameter (in mm) of blue-colored leaks from the site of injection at 1, 6 and 24 hours post administration of the test materials. The mm diameter of blueness at the site of injection is observed and recorded as well as the severity of the vascular leakage. 10 Blemishes of at least 5 mm in diameter are considered positive for the assay when testing purified proteins, being indicative of the ability to induce vascular leakage or permeability. A response greater than 7 mm diameter is considered positive for conditioned media samples. Human VEGF at 0.1 μ g/100 μ l is used as a positive control, inducing a response of 4-8 mm diameter.

The following PRO polypeptides tested positive in this assay: PRO1155.

15

EXAMPLE 168: Mouse Mesengial Cell Inhibition Assay (Assay 114)

This assay is designed to determine whether PRO polypeptides of the present invention show the ability to inhibit the proliferation of mouse mesengial cells in culture. PRO polypeptides testing positive in this assay would be expected to be useful for the therapeutic treatment of such diseases or conditions where 20 inhibition of mesengial cell proliferation would be beneficial such as, for example, cystic renal dysplasia, polycystic kidney disease, or other kidney disease assoiciated with abnormal mesengial cell proliferation, renal tumors, and the like.

On day 1, mouse mesengial cells are plated on a 96 well plate in growth medium (a 3:1 mixture of Dulbecco's modified Eagle's medium and Ham's F12 medium, 95%; fetal bovine serum, 5%; supplemented 25 with 14mM HEPES) and then are allowed to grow overnight. On day 2, the PRO polypeptide is diluted at 2 different concentrations (1%, 0.1%) in serum-free medium and is added to the cells. The negative control is growth medium without added PRO polypeptide. After the cells are allowed to incubate for 48 hours, 20 μ l of the Cell Titer 96 Aqueous one solution reagent (Promega) is added to each well and the colormetric reaction is allowed to proceed for 2 hours. The absorbance (OD) is then measured at 490 nm. A positive in the assay 30 is an absorbance reading which is at least 10% above the negative control.

The following PRO polypeptides tested positive in this assay: PRO1192 and PRO1195.

Example 169: *In Vitro* Antitumor Assay (Assay 161)

The antiproliferative activity of various PRO polypeptides was determined in the investigational, 35 disease-oriented *in vitro* anti-cancer drug discovery assay of the National Cancer Institute (NCI), using a sulforhodamine B (SRB) dye binding assay essentially as described by Skehan et al., *J. Natl. Cancer Inst.* 82:1107-1112 (1990). The 60 tumor cell lines employed in this study ("the NCI panel"), as well as conditions

for their maintenance and culture *in vitro* have been described by Monks et al., *J. Natl. Cancer Inst.* 83:757-766 (1991). The purpose of this screen is to initially evaluate the cytotoxic and/or cytostatic activity of the test compounds against different types of tumors (Monks et al., *supra*; Boyd, *Cancer: Princ. Pract. Oncol. Update* 3(10):1-12 [1989]).

Cells from approximately 60 human tumor cell lines were harvested with trypsin/EDTA (Gibco), 5 washed once, resuspended in IMEM and their viability was determined. The cell suspensions were added by pipet (100 μ L volume) into separate 96-well microtiter plates. The cell density for the 6-day incubation was less than for the 2-day incubation to prevent overgrowth. Inoculates were allowed a preincubation period of 24 hours at 37°C for stabilization. Dilutions at twice the intended test concentration were added at time zero 10 in 100 μ L aliquots to the microtiter plate wells (1:2 dilution). Test compounds were evaluated at five half-log dilutions (1000 to 100,000-fold). Incubations took place for two days and six days in a 5% CO₂ atmosphere and 100% humidity.

15 After incubation, the medium was removed and the cells were fixed in 0.1 ml of 10% trichloroacetic acid at 40°C. The plates were rinsed five times with deionized water, dried, stained for 30 minutes with 0.1 ml of 0.4% sulforhodamine B dye (Sigma) dissolved in 1% acetic acid, rinsed four times with 1% acetic acid to remove unbound dye, dried, and the stain was extracted for five minutes with 0.1 ml of 10 mM Tris base [tris(hydroxymethyl)aminomethane], pH 10.5. The absorbance (OD) of sulforhodamine B at 492 nm was measured using a computer-interfaced, 96-well microtiter plate reader.

A test sample is considered positive if it shows at least 50% growth inhibitory effect at one or more concentrations. The results are shown in the following table, where the abbreviations are as follows:

20 NSCL = non-small cell lung carcinoma

CNS = central nervous system

Table 7

	<u>Test compound</u>	<u>Concentration</u>	<u>Days</u>	<u>Tumor Cell Line Type</u>	<u>Cell Line Designation</u>
25	PRO1016	0.1 nM	2	Leukemia	K-568
	PRO1016	0.1 nM	2	Leukemia	MOLT-4
	PRO1016	0.1 nM	2	Leukemia	RPMI-8226
	PRO1016	0.1 nM	2	NSCL	A549/ATCC
30	PRO1016	0.1 nM	2	NSCL	EKVX
	PRO1016	0.1 nM	2	NSCL	NCI-H23
	PRO1016	0.1 nM	2	NSCL	NCI-H522
	PRO1016	0.1 nM	2	Colon	KM-12
	PRO1016	0.1 nM	2	CNS	SF-295
35	PRO1016	0.1 nM	2	Melanoma	SK-MEL-5
	PRO1016	0.1 nM	2	Melanoma	UACC-257
	PRO1016	0.1 nM	2	Ovarian	OVCAR-3
	PRO1016	0.1 nM	2	Ovarian	OVCAR-4
	PRO1016	0.1 nM	2	Breast	NCI/SDR-RES
40	PRO1016	0.1 nM	2	Breast	T-47D
	PRO1016	0.1 nM	6	Leukemia	CCRF-CEM
	PRO1016	0.1 nM	6	Leukemia	K-562

Table 7 (cont')

	<u>Test compound</u>	<u>Concentration</u>	<u>Days</u>	<u>Tumor Cell Line Type</u>	<u>Cell Line Designation</u>
5	PRO1016	0.1 nM	6	Leukemia	MOLT-4
	PRO1016	0.1 nM	6	Leukemia	RPMI-8226
	PRO1016	0.1 nM	6	NSCL	A549/ATCC
	PRO1016	0.1 nM	6	NSCL	EKVX
	PRO1016	0.1 nM	6	NSCL	HOP-62
	PRO1016	0.1 nM	6	NSCL	NCI-H23
10	PRO1016	0.1 nM	6	NSCL	NCI-H322M
	PRO1016	0.1 nM	6	NSCL	NCI-H460
	PRO1016	0.1 nM	6	NSCL	NCI-H522
	PRO1016	0.1 nM	6	Colon	COLO 205
	PRO1016	0.1 nM	6	Colon	CHT-116
	PRO1016	0.1 nM	6	Colon	HCT-15
15	PRO1016	0.1 nM	6	Colon	HT-29
	PRO1016	0.1 nM	6	Colon	SW-620
	PRO1016	0.1 nM	6	CNS	SF-295
	PRO1016	0.1 nM	6	CNS	SF-539
	PRO1016	0.1 nM	6	CNS	SNB-19
	PRO1016	0.1 nM	6	CNS	U251
20	PRO1016	0.1 nM	6	Melanoma	LOX IMVI
	PRO1016	0.1 nM	6	Melanoma	MALME-3M
	PRO1016	0.1 nM	6	Melanoma	SK-MEL-28
	PRO1016	0.1 nM	6	Melanoma	SK-MEL-5
	PRO1016	0.1 nM	6	Melanoma	UACC-257
	PRO1016	0.1 nM	6	Melanoma	UACC-62
25	PRO1016	0.1 nM	6	Ovarian	IGROV1
	PRO1016	0.1 nM	6	Ovarian	OVCAR-3
	PRO1016	0.1 nM	6	Ovarian	OVCAR-4
	PRO1016	0.1 nM	6	Ovarian	OVCAR-8
	PRO1016	0.1 nM	6	Renal	ACHN
	PRO1016	0.1 nM	6	Renal	RXF 393
30	PRO1016	0.1 nM	6	Renal	SN12C
	PRO1016	0.1 nM	6	Renal	TK-10
	PRO1016	0.1 nM	6	Prostate	PC-3
	PRO1016	0.1 nM	6	Breast	MCF-7
	PRO1016	0.1 nM	6	Breast	NCI/ADR-RES
	PRO1016	0.1 nM	6	Breast	MDA-MB-231
35	PRO1016	0.1 nM	6	Breast	MDA-MB-435
	PRO1016	0.1 nM	6	Breast	MDA-N
	PRO1016	0.1 nM	6	Breast	BT-549
	PRO1016	0.1 nM	6	Breast	T-47D
	PRO1186	95 nM	2	NSCL	NCI-H226
	PRO1186	95 nM	2	Colon	Colo205
40	PRO1186	2.2 nM	6	Breast	MDA-N
	PRO1186	114 nM	2	NSCL	NCI-H322M
	PRO1186	114 nM	2	CNS	SF-268; SF-539
	PRO1186	114 nM	2	Ovarian	IGFOV1
	PRO1186	114 nM	2	Renal	786-0; SN12C; TK-10
	PRO1186	114 nM	6	Leukemia	MOLT-4; RPMI-8226
45	PRO1186	114 nM	6	Melanoma	LOX IMVI
	PRO1186	114 nM	6	Ovarian	OVCAR-4; SK-OV-3
	PRO1186	114 nM	6		
	PRO1186	114 nM	6		
	PRO1186	114 nM	6		
	PRO1186	114 nM	6		
50	PRO1186	114 nM	6		
	PRO1186	114 nM	6		
	PRO1186	114 nM	6		
	PRO1186	114 nM	6		
	PRO1186	114 nM	6		
	PRO1186	114 nM	6		

<u>Table 7 (cont')</u>					
	<u>Test compound</u>	<u>Concentration</u>	<u>Days</u>	<u>Tumor Cell Line Type</u>	<u>Cell Line Designation</u>
5	PRO1186	114 nM	6	Breast	MDA-MB-435; T-47D
	PRO1186	8.1 nM	6	Leukemia	K-562
	PRO1186	8.1 nM	6	NSCL	HOP-62
	PRO1186	8.1 nM	6	Colon	Colo205; HCC-2998
	PRO1186	8.1 nM	6	Breast	T-47D
10	PRO1186	15.4 nM	6	Leukemia	K-562
	PRO1186	3.6 nM	2	Ovarian	OVCAR-3
	PRO1186	3.6 nM	6	NSCL	HOP-62

The results of these assays demonstrate that the positive testing PRO polypeptides are useful for inhibiting neoplastic growth in a number of different tumor cell types and may be used therapeutically therefor.. Antibodies against these PRO polypeptides are useful for affinity purification of these useful polypeptides. Nucleic acids encoding these PRO polypeptides are useful for the recombinant preparation of these polypeptides.

EXAMPLE 170: Gene Amplification in Tumors

20 This example shows that certain PRO polypeptide-encoding genes are amplified in the genome of certain human lung, colon and/or breast cancers and/or cell lines. Amplification is associated with overexpression of the gene product, indicating that the polypeptides are useful targets for therapeutic intervention in certain cancers such as colon, lung, breast and other cancers and diagnostic determination of the presence of those cancers. Therapeutic agents may take the form of antagonists of the PRO polypeptide, 25 for example, murine-human chimeric, humanized or human antibodies against a PRO polypeptide.

The starting material for the screen was genomic DNA isolated from a variety cancers. The DNA is quantitated precisely, *e.g.*, fluorometrically. As a negative control, DNA was isolated from the cells of ten normal healthy individuals which was pooled and used as assay controls for the gene copy in healthy individuals (not shown). The 5' nuclease assay (for example, TaqManTM) and real-time quantitative PCR (for 30 example, ABI Prism 7700 Sequence Detection SystemTM (Perkin Elmer, Applied Biosystems Division, Foster City, CA)), were used to find genes potentially amplified in certain cancers. The results were used to determine whether the DNA encoding the PRO polypeptide is over-represented in any of the primary lung or colon cancers or cancer cell lines or breast cancer cell lines that were screened. The primary lung cancers were obtained from individuals with tumors of the type and stage as indicated in Table 8. An explanation of 35 the abbreviations used for the designation of the primary tumors listed in Table 8 and the primary tumors and cell lines referred to throughout this example are given below.

The results of the TaqManTM are reported in delta (Δ) Ct units. One unit corresponds to 1 PCR cycle or approximately a 2-fold amplification relative to normal, two units corresponds to 4-fold, 3 units to 8-fold amplification and so on. Quantitation was obtained using primers and a TaqManTM fluorescent probe derived 40 from the PRO polypeptide-encoding gene. Regions of the PRO polypeptide-encoding gene which are most likely to contain unique nucleic acid sequences and which are least likely to have spliced out introns are

preferred for the primer and probe derivation, *e.g.*, 3'-untranslated regions. The sequences for the primers and probes (forward, reverse and probe) used for the PRO polypeptide gene amplification analysis were as follows:

PRO290 (DNA35680-1212):

35680.tm.p:

5 5'-CCACCAATGGCAGCCCCACCT-3' (SEQ ID NO:428)

35680.tm.f:

5'-GACTGCCCTCCCTGCCA-3' (SEQ ID NO:429)

35680.tm.r:

5'-CAAAAAGCCTGGAAGTCTTCAAAG-3' (SEQ ID NO:430)

10

PRO341 (DNA26288-1239):

26288.tm.f1:

5'-CAGCTGGACTGCAGGTGCTA-3' (SEQ ID NO:431)

26288.tm.r1:

15

5'-CAGTGAGCACAGCAAGTGTCCCT-3' (SEQ ID NO:432)

26288.tm.p1:

5'-GGCCACCTCCTTGAGTCTTCAGTCCCT-3' (SEQ ID NO:433)

PRO535 (DNA49143-1429):

20

49143.tm.f1:

5'-CAACTACTGGCTAAAGCTGGTGAA-3' (SEQ ID NO:434)

49143.tm.r1:

5'-CCTTCTGTATAGGTGATAACCAATGA-3' (SEQ ID NO:435)

49143.tm.p1:

25

5'-TGGCCATCCCTACCAGAGGCAGAA-3' (SEQ ID NO:436)

PRO619 (DNA49821-1562):

49821.tm.f1:

5'-CTGAAGACGACGCCGGATTACTA-3' (SEQ ID NO:437)

30

49821.tm.r1:

5'-GGCAGAAATGGGAGGCAGA-3' (SEQ ID NO:438)

49821.tm.p1:

5'-TGCTCTGTTGGCTACGGCTTAGTCCCTAG-3' (SEQ ID NO:439)

35

PRO809 (DNA57836-1338):

57836.tm.f1:

5'-AGCAGCAGCCATGTAGAATGAA-3' (SEQ ID NO:440)

57836.tm.r1:

5'-AATACGAACAGTGCACGCTGAT-3' (SEQ ID NO:441)

57836.tm.p1:

5'-TCCAGAGAGCCAAGCACGGCAGA-3' (SEQ ID NO:442)

5 PRO830 (DNA56866-1342):56866.tm.f1:

5'-TCTAGCCAGCTTGGCTCCAATA-3' (SEQ ID NO:443)

56866.tm.r1:

5'-CCTGGCTCTAGCACCAACTCATA-3' (SEQ ID NO:444)

10 56866.tm.p1:

5'-TCAGTGGCCCTAAGGAGATGGGCCT-3' (SEQ ID NO:445)

PRO848 (DNA59839-1461):59839.tm.f1:

15 5'-CAGGATACAGTGGGAATCTTGAGA-3' (SEQ ID NO:446)

59839.tm.r1:

5'-CCTGAAGGGCTTGGAGCTTAGT-3' (SEQ ID NO:447)

59839.tm.p1:

5'-TCTTGGCCATTCCCATGGCTCA-3' (SEQ ID NO:448)

20

PRO943 (DNA52192-1369):52192.tm.f1:

5'-CCCATGGCGAGGAGGAAT-3' (SEQ ID NO:449)

52192.tm.r1:

25 5'-TGCCTACGTGTGCCTTCAG-3' (SEQ ID NO:450)

52192.tm.p1:

5'-CAGCACCCAGGCAGTCTGTGTGT-3' (SEQ ID NO:451)

PRO1005 (DNA57708-1411):30 57708.tm.f1:

5'-AACGTGCTACACGACCAGTGTACT-3' (SEQ ID NO:452)

57708.tm.r1:

5'-CACAGCATATTAGATGACTAAATCCA-3' (SEQ ID NO:453)

57708.tm.p1:

35 5'-TTGTTTAGTTCTCCACCGTGTCTCCACAGAA-3' (SEQ ID NO:454)

PRO1009 (DNA57129-1413):57129.tm.fl:

5'-TGTCAGAATGCAACCTGGCTT-3' (SEQ ID NO:455)

57129.tm.rl:

5'-TGATGTGCCTGGCTCAGAAC-3' (SEQ ID NO:456)

5 57129.tm.p1:

5'-TGCACCTAGATGTCCCCAGCACCC-3' (SEQ ID NO:457)

PRO1097 (DNA59841-1460):59841.tm.fl:

10 5'-AAGATGCCAGGCTTCTTA-3' (SEQ ID NO:458)

59841.tm.rl:

5'-CTCCTGTACGGTCTGCTCACTTAT-3' (SEQ ID NO:459)

59841.tm.p1:

5'-TGGCTGTCAGTCCAGTGTGCATGG-3' (SEQ ID NO:460)

15

PRO1107 (DNA59606-1471):59606.tm.fl:

5'-GCATAGGGATAGATAAGATCCTGCTTTAT-3' (SEQ ID NO:461)

59606.tm.rl:

20 5'-CAAATTAAAGTACCCATCAGGAGAGAA-3' (SEQ ID NO:462)

59606.tm.p1:

5'-AAGTTGCTAAATATACATTATCTGCCAAGTCCA-3' (SEQ ID NO:463)

PRO1111 (DNA58721-1475):25 58721.tm.fl:

5'-GTGCTGCCACAAATTATGA-3' (SEQ ID NO:464)

58721.tm.rl:

5'-GTCCTTGGTATGGGTCTGAATTATAT-3' (SEQ ID NO:465)

58721.tm.p1:

30 5'-ACTCTCTGCACCCCACAGTCACCACTATCTC-3' (SEQ ID NO:466)

PRO1153 (DNA59842-1502):59842.tm.fl:

5'-CTGAGGAACCAGCCATGTCTCT-3' (SEQ ID NO:467)

35 59842.tm.rl:

5'-GACCAGATGCAGGTACAGGATGA-3' (SEQ ID NO:468)

59842_tm.p1:

5'-CTGCCCTTCAGTGATGCCAACCTT-3' (SEQ ID NO:469)

PRO1182 (DNA59848-1512):59848_tm.f1:

5'-GGGTGGAGGCTCACTGAGTAGA-3' (SEQ ID NO:470)

59848_tm.r1:

5'-CAATACAGGTAATGAAACTCTGCTTCTT-3' (SEQ ID NO:471)

59848_tm.p1:

5'-TCCTCTTAAGCATAGGCCATTTCTCAGTTAGACA-3' (SEQ ID NO:472)

10

PRO1184 (DNA59220-1514):59220_tm.f1:

5'-GGTGGTCTTGCTTGGTCTCAC-3' (SEQ ID NO:473)

59220_tm.r1:

15

5'-CCGTCGTTCAGAACATGAC-3' (SEQ ID NO:474)

59220_tm.p1:

5'-ACCGCCTACCGCTGTGCCCA-3' (SEQ ID NO:475)

PRO1187 (DNA62876-1517):

20

62876_tm.f1:

5'-CAGTAAAACCACAGGGCTGGATT-3' (SEQ ID NO:476)

62876_tm.r1:

5'-CCTGAGAGCAAGAAGGTTGAGAAT-3' (SEQ ID NO:477)

62876_tm.p1:

25

5'-TAGACAGGGACCATGGCCCGCA-3' (SEQ ID NO:478)

PRO1281 (DNA59820-1549):59820_tm.f1:

5'-TGGGCTGTAGAAGAGTTGTTG-3' (SEQ ID NO:479)

30

59820_tm.r1:

5'-TCCACACTTGGCCAGTTTAT-3' (SEQ ID NO:480)

59820_tm.p1:

5'-CCCAACTCTCCCTTTGGACCCT-3' (SEQ ID NO:481)

35

PRO1112 (DNA57702-1476):57702_tm.f1

5'-GTCCCTTCACTGTTAGAGCATGA-3' (SEQ ID NO:482)

57702.tm.p1

5'-ACTCTCCCCCTAACAGCCTCCTGAG-3' (SEQ ID NO:483)

57702.tm.r1

5'-GTGGTCAGGGCAGATCCTTT-3' (SEQ ID NO:484)

5 PRO1185 (DNA62881-1515):62881.tm.f1:

5'-ACAGATCCAGGAGAGACTCCACA -3' (SEQ ID NO:485)

62881.tm.p1:

5'-AGCGGCGCTCCAGCCTGAAT -3' (SEQ ID NO:486)

10 62881.tm.r1:

5'-CATGATTGGTCCTCAGTTCCATC -3' (SEQ ID NO:487)

PRO1245 (DNA64884-1527):64884.tm.f1:

15 5'-ATAGAGGGCTCCAGAAAGTG -3' (SEQ ID NO:488)

64884.tm.p1:

5'-CAGGGCCTTCAGGGCCTTCAC-3' (SEQ ID NO:489)

64884.tm.r1:

5'-GCTCAGCCAAACACTGTCA-3' (SEQ ID NO:490)

20 64884.tm.f2:

5'-GGGGCCCTGACAGTGTT -3' (SEQ ID NO:491)

64884.tm.p2:

5'-CTGAGCCGAGACTGGAGCATCTACAC-3' (SEQ ID NO:492)

64884.tm.r2:

25 5'-GTGGGCAGCGTCTTGTC-3' (SEQ ID NO:493)

The 5' nuclease assay reaction is a fluorescent PCR-based technique which makes use of the 5' exonuclease activity of Taq DNA polymerase enzyme to monitor amplification in real time. Two oligonucleotide primers (forward [.f] and reverse [.r]) are used to generate an amplicon typical of a PCR reaction. A third oligonucleotide, or probe (.p), is designed to detect nucleotide sequence located between the two PCR primers. The probe is non-extendible by Taq DNA polymerase enzyme, and is labeled with a reporter fluorescent dye and a quencher fluorescent dye. Any laser-induced emission from the reporter dye is quenched by the quenching dye when the two dyes are located close together as they are on the probe. During the amplification reaction, the Taq DNA polymerase enzyme cleaves the probe in a template-dependent manner. The resultant probe fragments disassociate in solution, and signal from the released reporter dye is free from the quenching effect of the second fluorophore. One molecule of reporter dye is liberated for each new molecule synthesized, and detection of the unquenched reporter dye provides the basis for quantitative interpretation of the data.

The 5' nuclease procedure is run on a real-time quantitative PCR device such as the ABI Prism 7700TM Sequence Detection. The system consists of a thermocycler, laser, charge-coupled device (CCD) camera and computer. The system amplifies samples in a 96-well format on a thermocycler. During amplification, laser-induced fluorescent signal is collected in real-time through fiber optics cables for all 96 wells, and detected at the CCD. The system includes software for running the instrument and for analyzing the data.

5' Nuclease assay data are initially expressed as Ct, or the threshold cycle. This is defined as the cycle at which the reporter signal accumulates above the background level of fluorescence. The Δ Ct values are used as quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results.

10 Table 8 describes the stage, T stage and N stage of various primary tumors which were used to screen the PRO polypeptide compounds of the invention.

Table 8
Primary Lung and Colon Tumor Profiles

	<u>Primary Tumor Stage</u>	<u>Stage</u>	<u>Other Stage</u>	<u>Dukes Stage</u>	<u>T Stage</u>	<u>N Stage</u>
5	Human lung tumor AdenoCa (SRCC724) [LT1]	IIA			T1	N1
	Human lung tumor SqCCa (SRCC725) [LT1a]	IIB			T3	N0
	Human lung tumor AdenoCa (SRCC726) [LT2]	IB			T2	N0
	Human lung tumor AdenoCa (SRCC727) [LT3]	IIIA			T1	N2
	Human lung tumor AdenoCa (SRCC728) [LT4]	IB			T2	N0
10	Human lung tumor SqCCa (SRCC729) [LT6]	IB			T2	N0
	Human lung tumor Aden/SqCCa (SRCC730) [LT7]	IA			T1	N0
	Human lung tumor AdenoCa (SRCC731) [LT9]	IB			T2	N0
	Human lung tumor SqCCa (SRCC732) [LT10]	IIB			T2	N1
	Human lung tumor SqCCa (SRCC733) [LT11]	IIA			T1	N1
15	Human lung tumor AdenoCa (SRCC734) [LT12]	IV			T2	N0
	Human lung tumor AdenoSqCCa (SRCC735) [LT13]	IIB			T2	N0
	Human lung tumor SqCCa (SRCC736) [LT15]	IB			T2	N0
	Human lung tumor SqCCa (SRCC737) [LT16]	IB			T2	N0
	Human lung tumor SqCCa (SRCC738) [LT17]	IIB			T2	N1
20	Human lung tumor SqCCa (SRCC739) [LT18]	IB			T2	N0
	Human lung tumor SqCCa (SRCC740) [LT19]	IB			T2	N0
	Human lung tumor LCCa (SRCC741) [LT21]	IIB			T3	N1
	Human lung AdenoCa (SRCC811) [LT22]	1A			T1	N0
	Human colon AdenoCa (SRCC742) [CT2]		M1	D	pT4	N0
25	Human colon AdenoCa (SRCC743) [CT3]			B	pT3	N0
	Human colon AdenoCa (SRCC744) [CT8]			B	T3	N0
	Human colon AdenoCa (SRCC745) [CT10]			A	pT2	N0
	Human colon AdenoCa (SRCC746) [CT12]		MO, R1	B	T3	N0
	Human colon AdenoCa (SRCC747) [CT14]		pMO, RO	B	pT3	pN0
30	Human colon AdenoCa (SRCC748) [CT15]		M1, R2	D	T4	N2
	Human colon AdenoCa (SRCC749) [CT16]		pMO	B	pT3	pN0
	Human colon AdenoCa (SRCC750) [CT17]			C1	pT3	pN1
	Human colon AdenoCa (SRCC751) [CT1]		MO, R1	B	pT3	N0
	Human colon AdenoCa (SRCC752) [CT4]			B	pT3	M0
35	Human colon AdenoCa (SRCC753) [CT5]		G2	C1	pT3	pN0
	Human colon AdenoCa (SRCC754) [CT6]		pMO, RO	B	pT3	pN0
	Human colon AdenoCa (SRCC755) [CT7]		G1	A	pT2	pN0
	Human colon AdenoCa (SRCC756) [CT9]		G3	D	pT4	pN2
	Human colon AdenoCa (SRCC757) [CT11]			B	T3	N0
40	Human colon AdenoCa (SRCC758) [CT18]		MO, RO	B	pT3	pN0

DNA Preparation:

DNA was prepared from cultured cell lines, primary tumors, normal human blood. The isolation was performed using purification kit, buffer set and protease and all from Quiagen, according to the manufacturer's instructions and the description below.

45 *Cell culture tysis:*

Cells were washed and trypsinized at a concentration of 7.5×10^8 per tip and pelleted by centrifuging at 1000 rpm for 5 minutes at 4°C, followed by washing again with 1/2 volume of PBS recentrifugation. The pellets were washed a third time, the suspended cells collected and washed 2x with PBS. The cells were then suspended into 10 ml PBS. Buffer C1 was equilibrated at 4°C. Qiagen protease #19155 was diluted into 6.25 ml cold ddH₂O to a final concentration of 20 mg/ml and equilibrated at 4°C. 10 ml of G2 Buffer was prepared

by diluting Qiagen RNase A stock (100 mg/ml) to a final concentration of 200 μ g/ml.

5 Buffer C1 (10 ml, 4°C) and ddH₂O (40 ml, 4°C) were then added to the 10 ml of cell suspension, mixed by inverting and incubated on ice for 10 minutes. The cell nuclei were pelleted by centrifuging in a Beckman swinging bucket rotor at 2500 rpm at 4°C for 15 minutes. The supernatant was discarded and the nuclei were suspended with a vortex into 2 ml Buffer C1 (at 4°C) and 6 ml ddH₂O, followed by a second 4°C centrifugation at 2500 rpm for 15 minutes. The nuclei were then resuspended into the residual buffer using 200 μ l per tip. G2 buffer (10 ml) was added to the suspended nuclei while gentle vortexing was applied. Upon completion of buffer addition, vigorous vortexing was applied for 30 seconds. Quiagen protease (200 μ l, prepared as indicated above) was added and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until the lysates were clear (e.g., incubating additional 30-60 minutes, pelleting at 10

10 3000 x g for 10 min., 4°C).

Solid human tumor sample preparation and lysis:

Tumor samples were weighed and placed into 50 ml conical tubes and held on ice. Processing was limited to no more than 250 mg tissue per preparation (1 tip/preparation). The protease solution was freshly prepared by diluting into 6.25 ml cold ddH₂O to a final concentration of 20 mg/ml and stored at 4°C. G2 15 buffer (20 ml) was prepared by diluting DNase A to a final concentration of 200 mg/ml (from 100 mg/ml stock). The tumor tissue was homogenated in 19 ml G2 buffer for 60 seconds using the large tip of the polytron in a laminar-flow TC hood in order to avoid inhalation of aerosols, and held at room temperature. Between samples, the polytron was cleaned by spinning at 2 x 30 seconds each in 2L ddH₂O, followed by G2 buffer (50 ml). If tissue was still present on the generator tip, the apparatus was disassembled and cleaned.

20 Quiagen protease (prepared as indicated above, 1.0 ml) was added, followed by vortexing and incubation at 50°C for 3 hours. The incubation and centrifugation was repeated until the lysates were clear (e.g., incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

Human blood preparation and lysis:

Blood was drawn from healthy volunteers using standard infectious agent protocols and citrated into 25 10 ml samples per tip. Quiagen protease was freshly prepared by dilution into 6.25 ml cold ddH₂O to a final concentration of 20 mg/ml and stored at 4°C. G2 buffer was prepared by diluting RNase A to a final concentration of 200 μ g/ml from 100 mg/ml stock. The blood (10 ml) was placed into a 50 ml conical tube and 10 ml C1 buffer and 30 ml ddH₂O (both previously equilibrated to 4°C) were added, and the components mixed by inverting and held on ice for 10 minutes. The nuclei were pelleted with a Beckman swinging bucket 30 rotor at 2500 rpm, 4°C for 15 minutes and the supernatant discarded. With a vortex, the nuclei were suspended into 2 ml C1 buffer (4°C) and 6 ml ddH₂O (4°C). Vortexing was repeated until the pellet was white. The nuclei were then suspended into the residual buffer using a 200 μ l tip. G2 buffer (10 ml) were added to the suspended nuclei while gently vortexing, followed by vigorous vortexing for 30 seconds. Quiagen protease was added (200 μ l) and incubated at 50°C for 60 minutes. The incubation and centrifugation was repeated until 35 the lysates were clear (e.g., incubating additional 30-60 minutes, pelleting at 3000 x g for 10 min., 4°C).

Purification of cleared lysates:(1) Isolation of genomic DNA:

Genomic DNA was equilibrated (1 sample per maxi tip preparation) with 10 ml QBT buffer. QF elution buffer was equilibrated at 50°C. The samples were vortexed for 30 seconds, then loaded onto equilibrated tips and drained by gravity. The tips were washed with 2 x 15 ml QC buffer. The DNA was 5 eluted into 30 ml silanized, autoclaved 30 ml Corex tubes with 15 ml QF buffer (50°C). Isopropanol (10.5 ml) was added to each sample, the tubes covered with parafin and mixed by repeated inversion until the DNA precipitated. Samples were pelleted by centrifugation in the SS-34 rotor at 15,000 rpm for 10 minutes at 4°C. The pellet location was marked, the supernatant discarded, and 10 ml 70% ethanol (4°C) was added. Samples were pelleted again by centrifugation on the SS-34 rotor at 10,000 rpm for 10 minutes at 4°C. The pellet 10 location was marked and the supernatant discarded. The tubes were then placed on their side in a drying rack and dried 10 minutes at 37°C, taking care not to overdry the samples.

After drying, the pellets were dissolved into 1.0 ml TE (pH 8.5) and placed at 50°C for 1-2 hours. Samples were held overnight at 4°C as dissolution continued. The DNA solution was then transferred to 1.5 ml tubes with a 26 gauge needle on a tuberculin syringe. The transfer was repeated 5x in order to shear the 15 DNA. Samples were then placed at 50°C for 1-2 hours.

(2) Quantitation of genomic DNA and preparation for gene amplification assay:

The DNA levels in each tube were quantified by standard A_{260} , A_{280} spectrophotometry on a 1:20 dilution (5 μ l DNA + 95 μ l ddH₂O) using the 0.1 ml quartz cuvets in the Beckman DU640 spectrophotometer. A_{260}/A_{280} ratios were in the range of 1.8-1.9. Each DNA samples was then diluted further 20 to approximately 200 ng/ml in TE (pH 8.5). If the original material was highly concentrated (about 700 ng/ μ l), the material was placed at 50°C for several hours until resuspended.

Fluorometric DNA quantitation was then performed on the diluted material (20-600 ng/ml) using the manufacturer's guidelines as modified below. This was accomplished by allowing a Hoeffer DyNA Quant 200 fluorometer to warm-up for about 15 minutes. The Hoechst dye working solution (#H33258, 10 μ l, prepared 25 within 12 hours of use) was diluted into 100 ml 1 x TNE buffer. A 2 ml cuvette was filled with the fluorometer solution, placed into the machine, and the machine was zeroed. pGEM 3Zf(+) (2 μ l, lot #360851026) was added to 2 ml of fluorometer solution and calibrated at 200 units. An additional 2 μ l of pGEM 3Zf(+) DNA was then tested and the reading confirmed at 400 +/- 10 units. Each sample was then 30 read at least in triplicate. When 3 samples were found to be within 10% of each other, their average was taken and this value was used as the quantification value.

The fluorometrically determined concentration was then used to dilute each sample to 10 ng/ μ l in ddH₂O. This was done simultaneously on all template samples for a single TaqMan plate assay, and with enough material to run 500-1000 assays. The samples were tested in triplicate with Taqman™ primers and probe both B-actin and GAPDH on a single plate with normal human DNA and no-template controls. The 35 diluted samples were used provided that the CT value of normal human DNA subtracted from test DNA was +/- 1 Ct. The diluted, lot-qualified genomic DNA was stored in 1.0 ml aliquots at -80°C. Aliquots which were subsequently to be used in the gene amplification assay were stored at 4°C. Each 1 ml aliquot is enough

for 8-9 plates or 64 tests.

Gene amplification assay:

The PRO polypeptide compounds of the invention were screened in the following primary tumors and the resulting ΔCt values greater than or equal to 1.0 are reported in Tables 9A-C below.

Table 9A
ΔCt values in lung and colon primary tumors and cell line models

Primary Tumor	PRO290	PRO341	PRO355	PRO619	PRO1112	PRO309	PRO830	PRO848
LT-1a	—	—	—	—	—	—	—	—
LT3	—	—	—	1.04	—	—	—	—
LT7	—	—	—	1.68	—	—	—	—
LT9	—	—	—	1.21	—	—	—	—
LT10	—	—	—	1.34	—	—	—	—
LT11	1.63	—	1.40	1.69	1.525	1.40	1.25	1.04
LT12	—	—	—	1.57	—	—	—	—
LT13	1.47	—	1.37	1.81	1.195	1.61	1.35	1.22
LT15	1.67	—	—	2.13	1.635	1.03	—	—
LT16	—	—	1.12	1.74	—	—	—	—
LT17	1.22	1.33	1.42	2.08	1.775	—	—	—
LT18	—	—	—	1.52	—	—	—	—
LT19	2.07	—	—	1.14	—	—	—	—
LT21	—	—	1.15	1.32	1.255	—	—	—
CT2	1.56	—	—	1.14	—	—	—	—
				2.33	—	—	1.31	—
				1.67	—	—	—	—
				1.90	—	—	—	—
				1.15	—	1.05	—	1.07
				1.09	—	—	—	—
				1.22	2.265	—	—	—

Table 9A (cont')
 ΔCt values in lung and colon primary tumors and cell line models

Primary Tumor	PRO290	PRO341	PRO535	PRO619	PRO1112	PRO809	PRO830	PRO848
CT3	--	--	1.28	1.49	--	--	--	--
CT8	--	--	--	--	1.065	--	--	--
CT10	--	--	1.34	--	1.575	--	--	--
CT12	--	--	--	--	1.315	--	--	--
CT14	--	--	1.29	--	1.895	--	--	--
CT15	--	--	1.10	1.00	1.465	--	--	--
CT16	--	--	1.35	1.02	1.255	--	--	--
CT17	--	--	1.26	1.23	--	--	--	--
CT1	--	--	--	1.12	1.245	--	--	--
CT4	--	--	1.03	1.25	1.535	--	--	--
CT5	--	--	--	1.34	1.975	--	--	--
CT6	--	--	1.00	1.06	1.575	--	--	--
CT11	1.16	--	1.25	1.80	2.285	--	--	--

Table 9B
 Δ C_t values in lung and colon primary tumors and cell line models

Primary Tumor	PRO943	PRO1005	PRO1009	PRO1185	PRO1245	PRO1097	PRO1107	PRO1111	PRO1153
LT-1	--	1.07	--	--	--	--	--	--	--
LT-1a	--	3.87	--	--	--	--	--	--	--
LT2	--	--	--	--	--	1.23	--	--	--
LT3	--	1.61	--	1.01	--	--	--	1.39	--
LT4	--	--	--	--	--	--	--	1.49	1.01
LT6	--	1.29	--	--	--	--	--	--	--
LT7	--	--	--	--	--	--	--	1.58	1.52
LT9	--	2.50	--	--	--	1.21	--	1.44	--
LT10	--	--	--	--	--	--	--	1.05	--
LT11	2.06	--	--	--	--	--	--	1.45	--
LT12	1.94	1.21	--	--	--	--	--	--	--
LT13	1.64	2.30	--	--	3.84	--	3.55	--	--
	1.27								
LT15	2.05	1.03	--	--	1.01	--	2.47	--	--
LT16	--	1.05	--	--	1.98	--	2.45	--	--
LT17	1.93	--	--	--	--	--	--	1.47	--
LT19	2.90	--	--	--	--	--	--	--	--
LT26	--	--	--	--	1.66	--	--	--	--
LT30	--	--	--	--	1.58	--	--	--	--
CT2	1.92	--	2.00	1.73	--	--	4.75	--	--
CT3	--	--	1.75	--	--	--	1.52	--	--
CT8	1.37	--	1.29	--	--	--	--	--	--
	1.12								

Table 9B (cont')
 ΔCt values in lung and colon primary tumors and cell line models

Primary Tumor	PRO943	PRO1005	PRO1009	PRO1185	PRO1245	PRO1097	PRO1107	PRO1111	PRO1153
CT10	2.13	--	1.73	--	--	--	2.82	--	--
	1.67								
CT12	1.43	--	1.92	--	--	--	--	--	--
CT14	1.46	--	2.10	--	--	1.08	1.54	1.38	--
CT15	--	--	2.02	--	1.00	--	--	--	--
CT16	--	--	1.56	--	--	1.11	--	--	--
CT17	1.30	--	1.76	--	--	1.34	--	--	--
CT1	1.36	--	--	--	--	--	1.57	--	--
CT4	--	--	1.06	--	--	--	1.59	--	--
CT5	1.88	--	1.43	--	--	--	--	--	--
CT6	1.41	--	--	--	--	--	--	--	--
	2.51								
	1.75								
CT7	--	--	--	--	--	--	--	1.16	--
CT11	2.80	--	1.83	--	--	--	--	1.17	--
	2.61								
	1.30	--	--	--	--	--	1.05	--	--
HS22	--	--	--	--	1.10	--	--	--	--

Table 9C
ΔCt values in lung and colon primary tumors and cell line models

Primary Tumor	PRO1182	PRO1184	PRO1187	PRO1281
5				
LT-1	1.81	—	—	—
LT-1a	—	1.14	—	—
		1.09		
LT4	1.43	1.37	—	—
10		1.18		
LT6	—	1.78	—	—
		1.66		
		1.05		
LT9	1.43	—	—	—
15	LT12	—	2.47	1.17
			2.61	—
			1.80	
LT15	—	—	1.55	—
20	LT16	—	1.01	1.33
	LT17	—	—	—
	LT18	—	1.07	—
			1.13	
25	LT19	—	1.19	—
			1.35	—
			1.02	
LT21	—	1.00	—	—
			1.20	
30	CT2	—	—	1.15
	CT12	—	—	1.07

Because amplification of the various DNAs described above occurs in various cancerous tumors and tumor cell lines derived from various human tissues, these molecules likely play a significant role in tumor formation and/or growth. As a result, amplification and/or enhanced expression of these molecules can serve as a diagnostic for detecting the presence of tumor in an individual and antagonists (e.g., antibodies) directed against the proteins encoded by the above described DNA molecules would be expected to have utility in cancer therapy.

EXAMPLE 171: Identification of Receptor/Ligand Interactions

In this assay, various PRO polypeptides are tested for ability to bind to a panel of potential receptor molecules for the purpose of identifying receptor/ligand interactions. The identification of a ligand for a known receptor, a receptor for a known ligand or a novel receptor/ligand pair is useful for a variety of indications including, for example, targeting bioactive molecules (linked to the ligand or receptor) to a cell known to express the receptor or ligand, use of the receptor or ligand as a reagent to detect the presence of the ligand or receptor in a composition suspected of containing the same, wherein the composition may comprise cells suspected of expressing the ligand or receptor, modulating the growth of or another biological or immunological activity of a cell known to express or respond to the receptor or ligand, modulating the immune response of cells or toward cells that express the receptor or ligand, allowing the preparation of agonists, antagonists and/or antibodies directed against the receptor or ligand which will modulate the growth of or a biological or immunological activity of a cell expressing the receptor or ligand, and various other indications which will be readily apparent to the ordinarily skilled artisan.

The assay is performed as follows. A PRO polypeptide of the present invention suspected of being a ligand for a receptor is expressed as a fusion protein containing the Fc domain of human IgG (an immunoadhesin). Receptor-ligand binding is detected by allowing interaction of the immunoadhesin polypeptide with cells (e.g. Cos cells) expressing candidate PRO polypeptide receptors and visualization of bound immunoadhesin with fluorescent reagents directed toward the Fc fusion domain and examination by microscope. Cells expressing candidate receptors are produced by transient transfection, in parallel, of defined subsets of a library of cDNA expression vectors encoding PRO polypeptides that may function as receptor molecules. Cells are then incubated for 1 hour in the presence of the PRO polypeptide immunoadhesin being tested for possible receptor binding. The cells are then washed and fixed with paraformaldehyde. The cells are then incubated with fluorescent conjugated antibody directed against the Fc portion of the PRO polypeptide immunoadhesin (e.g. FITC conjugated goat anti-human-Fc antibody). The cells are then washed again and examined by microscope. A positive interaction is judged by the presence of fluorescent labeling of cells transfected with cDNA encoding a particular PRO polypeptide receptor or pool of receptors and an absence of similar fluorescent labeling of similarly prepared cells that have been transfected with other cDNA or pools of cDNA. If a defined pool of cDNA expression vectors is judged to be positive for interaction with a PRO polypeptide immunoadhesin, the individual cDNA species that comprise the pool are tested individually (the pool is "broken down") to determine the specific cDNA that encodes a receptor able to interact with the PRO polypeptide immunoadhesin.

In another embodiment of this assay, an epitope-tagged potential ligand PRO polypeptide (e.g. 8 histidine "His" tag) is allowed to interact with a panel of potential receptor PRO polypeptide molecules that have been expressed as fusions with the Fc domain of human IgG (immunoadhesins). Following a 1 hour co-incubation with the epitope tagged PRO polypeptide, the candidate receptors are each immunoprecipitated with protein A beads and the beads are washed. Potential ligand interaction is determined by western blot analysis of the immunoprecipitated complexes with antibody directed towards the epitope tag. An interaction is judged to occur if a band of the anticipated molecular weight of the epitope tagged protein is observed in the western blot analysis with a candidate receptor, but is not observed to occur with the other members of the panel of potential receptors.

Using these assays, the following receptor/ligand interactions have been herein identified:

10 (1) PRO943 binds to FHF1, PRO183 (FHF2), PRO184 (FHF3) and PRO185 (FHF4) and vice versa.
(2) PRO331 binds to PRO1133 and vice versa.
(3) PRO363 binds to PRO1387 and vice versa.
(4) PRO5723 binds to PRO1387 and vice versa.
(5) PRO1114 binds to PRO3301 and PRO9940 and vice versa.

15 (6) PRO9828 appears to be a novel fibroblast growth factor receptor (FGFR) ligand in that it binds to the known FGF receptors FGFR1, FGFR2IIIC, FGFR3IIIC and FGFR4. PRO9828 and agonists, therefore, will find use for activating the biological activities normally activated by FGF molecules including, for example, cell growth and proliferation. Antagonists of PRO9828 will find use in blocking the biological activities mediated through the FGF receptor.

20 (7) PRO1181 binds to PRO7170, PRO361 and PRO846.

EXAMPLE 172: Tissue Expression Distribution

Oligonucleotide probes were constructed from the PRO polypeptide-encoding nucleotide sequences shown in the figures for use in quantitative PCR amplification reactions. The oligonucleotide probes were chosen so as to give an approximately 200-600 base pair amplified fragment from the 3' end of its associated template in a standard PCR reaction. The oligonucleotide probes were employed in standard quantitative PCR amplification reactions with cDNA libraries isolated from different human adult and/or fetal tissue sources and analyzed by agarose gel electrophoresis so as to obtain a quantitative determination of the level of expression of the PRO polypeptide-encoding nucleic acids in the various tissues tested. Knowledge of the expression pattern or the differential expression of the PRO polypeptide-encoding nucleic acids in various different human tissue types provides a diagnostic marker useful for tissue typing, with or without other tissue-specific markers, for determining the primary tissue source of a metastatic tumor, disease diagnosis, and the like. These assays provided the following results.

	<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
35	DNA16422-1209	substantia nigra, dendrocytes, uterus	hippocampus
	DNA16435-1208	substantia nigra, dendrocytes, uterus	hippocampus
	DNA26843-1389	dendrocytes, heart, uterus, colon tumor	hippocampus, substantia nigra, cartilage

	<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
	DNA26844-1394	HUVEC, dendrocytes, cartilage	substantia nigra, hippocampus, uterus, prostate
5	DNA40621-1440	prostate, uterus, colon tumor	brain, heart, HUVEC, cartilage
	DNA44161-1434	colon tumor, dendrocytes	substantia nigra, hippocampus, prostate, uterus
	DNA44694-1500	dendrocytes, hippocampus, prostate	colon tumor, substantia nigra, heart
	DNA48320-1433	prostate, uterus	colon tumor, brain, heart, cartilage
	DNA49647-1398	brain, heart, prostate, uterus	cartilage
10	DNA53913-1490	hippocampus	substantia nigra, dendrocytes
	DNA53978-1443	dendrocytes, uterus, prostate	substantia nigra, colon tumor
	DNA53996-1442	spleen, prostate, uterus, hippocampus	substantia nigra, heart
	DNA56050-1455	prostate, uterus, cartilage, hippocampus	heart, colon tumor, dendrocytes
	DNA56110-1437	spleen, colon tumor, brain, prostate	heart
15	DNA56410-1414	uterus, dendrocytes	hippocampus, substantia nigra, heart
	DNA56436-1448	substantia nigra, prostate, hippocampus	dendrocytes, heart, HUVEC
	DNA56855-1447	prostate, uterus	brain, cartilage, heart, colon tumor
	DNA56860-1510	colon tumor	prostate, uterus, dendrocytes
	DNA56868-1478	colon tumor, prostate	uterus, brain, heart, cartilage
	DNA56869-1545	prostate, uterus, cartilage	brain, colon tumor, spleen, heart
20	DNA57699-1412	dendrocytes, hippocampus, prostate	substantia nigra, heart
	DNA57704-1452	brain, heart, spleen, uterus, prostate	colon tumor
	DNA57710-1451	dendrocytes, hippocampus, spleen, uterus	substantia nigra, heart
	DNA57711-1501	dendrocytes, hippocampus, heart, cartilage	substantia nigra
25	DNA57827-1493	colon tumor, hippocampus, prostate	substantia nigra, dendrocytes, uterus
	DNA58723-1588	substantia nigra, cartilage, uterus	hippocampus, dendrocytes, HUVEC
	DNA58743-1609	brain, prostate, uterus	colon tumor, heart, spleen, cartilage
	DNA58846-1409	hippocampus, dendrocytes	substantia nigra, uterus, prostate, colon tumor
30	DNA58849-1494	prostate	brain, uterus, cartilage, heart, colon tumor
	DNA58850-1495	spleen, prostate, dendrocytes	hippocampus, substantia nigra, colon tumor
	DNA59213-1487	spleen, cartilage, prostate, substantia nigra	heart, hippocampus, dendrocytes
35	DNA59497-1496	dendrocytes, prostate, uterus, heart	cartilage, hippocampus, substantia nigra
	DNA59605-1418	dendrocytes, prostate, uterus	hippocampus, substantia nigra, colon tumor
	DNA59609-1470	dendrocytes	substantia nigra, hippocampus, heart, prostate, uterus, spleen
40	DNA59612-1466	prostate, dendrocytes	hippocampus, substantia nigra, uterus, colon tumor
	DNA59616-1465	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA59619-1464	dendrocytes, substantia nigra, colon tumor	hippocampus
45	DNA59625-1498	brain, colon tumor, prostate, uterus	THP-1 macrophages
	DNA59827-1426	substantia nigra, prostate, uterus	hippocampus, dendrocytes, heart
	DNA59828-1608	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA59853-1505	prostate	brain, uterus, spleen, heart, colon tumor
50	DNA59854-1459	cartilage	prostate, brain, heart, colon tumor
	DNA60283-1484	dendrocytes, spleen, prostate, uterus	hippocampus, substantia nigra, heart
	DNA60619-1482	dendrocytes, substantia nigra, colon tumor	hippocampus
	DNA60625-1507	cartilage	prostate, brain, heart, colon tumor
	DNA60629-1481	uterus, colon tumor, substantia nigra	hippocampus, dendrocytes, spleen, prostate
55	DNA61755-1554	dendrocytes, substantia nigra, colon tumor	hippocampus

<u>DNA Molecule</u>	<u>Tissues w/ Significant Expression</u>	<u>Tissues w/o Significant Expression</u>
DNA64852-1589	prostate, uterus	brain, heart, cartilage, colon tumor
DNA66308-1537	prostate, heart, uterus	brain, colon tumor, cartilage
DNA68869-1610	spleen, prostate, heart, uterus, colon tumor, substantia nigra	hippocampus, dendrocytes, prostate

5

EXAMPLE 173: Isolation of cDNA Clones Encoding Human PRO846

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA39949. Based on the DNA39949 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO846.

10

Forward and reverse PCR primers were synthesized:

forward PCR primer 5'-CCCTGCAGTGCACCTACAGGGAAG-3' (SEQ ID NO:518)

reverse PCR primer 5'-CTGTCTTCCCTGCTTGGCTGTGG-3' (SEQ ID NO:519)

15

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA39949 sequence which had the following nucleotide sequence

hybridization probe

5'-GGTGCAGGAAGGGTGGGATCCTCTTCTCGCTGCTCTGGCCACATC-3'

(SEQ ID NO:520)

20

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then used to isolate clones encoding the PRO846 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

25

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO846 [herein designated as DNA44196-1353] (SEQ ID NO:516) and the derived protein sequence for PRO846.

30

The entire nucleotide sequence of UNQ422 (DNA44196-1353) is shown in Figure 329 (SEQ ID NO:516). Clone UNQ422 (DNA44196-1353) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 25-27 and ending at the stop codon at nucleotide positions 1021-1023 (Figure 329). The predicted polypeptide precursor is 332 amino acids long (Figure 330). The full-length PRO846 protein shown in Figure 330 has an estimated molecular weight of about 36,143 daltons and a pI of about 5.89. Important regions of the amino acid sequence of PRO846 include the signal peptide, the transmembrane domain, an N-glycosylation site, a sequence typical of fibrinogen beta and gamma chains C-terminal domain, and a sequence typical of Ig like V-type domain as shown in Figure 330. Clone UNQ422 (DNA44196-1353) has been deposited with ATCC and is assigned ATCC deposit no. 209847.

35

EXAMPLE 174: Isolation of cDNA Clones Encoding Human PRO363

A consensus sequence was obtained relative to a variety of EST sequences as described in Example 1 above, wherein the consensus sequence obtained is herein designated DNA42828. Based on the DNA42828 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO363.

5

A pair of PCR primers (forward and reverse) were synthesized:

forward PCR primer (42828.f1) 5'-CCAGTGCACAGCAGGCAACGAAGC-3' (SEQ ID NO:521)

reverse PCR primer (42828.r1) 5'-ACTAGGCTGTATGCCTGGGTGGC-3' (SEQ ID NO:522)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus DNA42828

10

sequence which had the following nucleotide sequence

hybridization probe (42828.p1)

5'-GTATGTACAAAGCATCGGCATGGTTCAGGAGCAGTGACAGGC-3' (SEQ ID NO:523)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with the PCR primer pair identified above. A positive library was then used 15 to isolate clones encoding the PRO363 gene using the probe oligonucleotide and one of the PCR primers. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue (LIB227).

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO363 [herein designated as UNQ318 (DNA45419-1252)] (SEQ ID NO:500) and the derived protein sequence for PRO363.

20

The entire nucleotide sequence of UNQ318 (DNA45419-1252) is shown in Figure 313 (SEQ ID NO:500). Clone UNQ318 (DNA45419-1252) contains a single open reading frame with an apparent translational initiation site at nucleotide positions 190-192 and ending at the stop codon at nucleotide positions 1309-1311 (Figure 313). The predicted polypeptide precursor is 373 amino acids long (Figure 314). The full-length PRO363 protein shown in Figure 314 has an estimated molecular weight of about 41,281 daltons and 25 a pI of about 8.33. A transmembrane domain exists at amino acids 221 to 254 of the amino acid sequence shown in Figure 314 (SEQ ID NO:501). The PRO363 polypeptide also possesses at least two myelin P0 protein domains from about amino acids 15 to 56 and from about amino acids 87 to 116. Clone UNQ318 (DNA45419-1252) has been deposited with ATCC on February 5, 1998 and is assigned ATCC deposit no. 209616.

30

Analysis of the amino acid sequence of the full-length PRO363 polypeptide suggests that it possesses significant sequence similarity to the cell surface protein HCAR, thereby indicating that PRO363 may be a novel HCAR homolog. More specifically, an analysis of the Dayhoff database (version 35.45 SwissProt 35) evidenced significant homology between the PRO363 amino acid sequence and the following Dayhoff sequences, HS46KDA_1, HSU90716_1, MMCARH_1, MMCARHOM_1, MMU90715_1, A33_HUMAN, 35 P_W14146, P_W14158, A42632 and B42632.

EXAMPLE 175: Isolation of cDNA Clones Encoding a Human PRO9828

A consensus DNA sequence was assembled relative to other nucleic sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA139814. Based on the DNA139814 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO9828. Forward and reverse PCR primers generally range from 20 to 30 nucleotides and are often designed to give a PCR product of about 100-1000 bp in length. The probe sequences are typically 40-55 bp in length. In some cases, additional oligonucleotides are synthesized when the consensus sequence is greater than about 1-1.5 kbp. In order to screen several libraries for a full-length clone, DNA from the libraries was screened by PCR amplification, as per Ausubel et al., *Current Protocols in Molecular Biology, supra*, with the PCR primer pair. A positive library was then used to isolate clones encoding the gene of interest using the probe oligonucleotide and one of the primer pairs.

PCR primers (forward and reverse) were synthesized:

5'-AATCTCAGCACCAGCCACTCAGAGCA-3' (SEQ ID NO:524)

5'-GTTAAAGAGGGTGCCCTTCCAGCGA-3' (SEQ ID NO:525)

10 5'-TATCCAATGCCTCCCCACTGCTC-3' (SEQ ID NO:526)

5'-GATGAACTTGGCGAAGGGGCGGCA-3' (SEQ ID NO:527)

RNA for construction of the cDNA libraries was isolated from human fetal liver tissue. The cDNA libraries used to isolate the cDNA clones were constructed by standard methods using commercially available reagents such as those from Invitrogen, San Diego, CA. The cDNA was primed with oligo dT containing a 20 NotI site, linked with blunt to Sall hemikinased adaptors, cleaved with NotI, sized appropriately by gel electrophoresis, and cloned in a defined orientation into a suitable cloning vector (such as pRKB or pRKD; pRK5B is a precursor of pRK5D that does not contain the SfiI site; see, Holmes et al., *Science*, 253:1278-1280 (1991)) in the unique XhoI and NotI sites.

25 DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for a full-length PRO9828 polypeptide (designated herein as DNA142238-2768 [Figure 323, SEQ ID NO:510]) and the derived protein sequence for that PRO9828 polypeptide.

The full length clone identified above contained a single open reading frame with an apparent translational initiation site at nucleotide positions 232-234 and a stop signal at nucleotide positions 985-987 (Figure 323, SEQ ID NO:510). The predicted polypeptide precursor is 251 amino acids long, has a calculated 30 molecular weight of approximately 27,954 daltons and an estimated pI of approximately 9.22. Analysis of the full-length PRO9828 sequence shown in Figure 324 (SEQ ID NO:511) evidences the presence of a variety of important polypeptide domains as shown in Figure 324, wherein the locations given for those important polypeptide domains are approximate as described above. Chromosome mapping evidences that the PRO9828-encoding nucleic acid maps to chromosome 12p13 in humans. Clone DNA142238-2768 has been deposited 35 with ATCC on October 5, 1999 and is assigned ATCC deposit no. 819-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 324 (SEQ ID NO:511), evidenced sequence

identity between the PRO9828 amino acid sequence and the following Dayhoff sequences: P_Y08581, AB018122_1, FGF3_HUMAN, P_R70824, S54407, P_R80780, P_Y23761, P_W92312, OMFGF6_1 and P_R80871.

EXAMPLE 176: Isolation of cDNA Clones Encoding a Human PRO7170

5 DNA108722-2743 was identified by applying a proprietary signal sequence finding algorithm developed by Genentech, Inc. (South San Francisco, CA) upon ESTs as well as clustered and assembled EST fragments from public (e.g., Genbank) and/or private (LIFESEQ®, Incyte Pharmaceuticals, Inc., Palo Alto, CA) databases. The signal sequence algorithm computes a secretion signal score based on the character of the DNA nucleotides surrounding the first and optionally the second methionine codon(s) (ATG) at the 5'-end of
10 the sequence or sequence fragment under consideration. The nucleotides following the first ATG must code for at least 35 unambiguous amino acids without any stop codons. If the first ATG has the required amino acids, the second is not examined. If neither meets the requirement, the candidate sequence is not scored. In order to determine whether the EST sequence contains an authentic signal sequence, the DNA and corresponding amino acid sequences surrounding the ATG codon are scored using a set of seven sensors
15 (evaluation parameters) known to be associated with secretion signals.

Use of the above described signal sequence algorithm allowed identification of an EST cluster sequence from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, designated herein as CLU57836. This EST cluster sequence was then compared to a variety of expressed sequence tag (EST) databases which included public EST databases (e.g., Genbank) and a proprietary EST DNA database (LIFESEQ®, Incyte 20 Pharmaceuticals, Palo Alto, CA) to identify existing homologies. The homology search was performed using the computer program BLAST or BLAST2 (Altshul et al., *Methods in Enzymology* 266:460-480 (1996)). Those comparisons resulting in a BLAST score of 70 (or in some cases 90) or greater that did not encode known proteins were clustered and assembled into a consensus DNA sequence with the program "phrap" (Phil 25 Green, University of Washington, Seattle, Washington). The consensus sequence obtained therefrom is herein designated DNA58756.

In light of an observed sequence homology between the DNA58756 sequence and an EST sequence encompassed within clone no. 2251462 from the LIFESEQ® database, Incyte Pharmaceuticals, Palo Alto, CA, clone no. 2251462 was purchased and the cDNA insert was obtained and sequenced. It was found herein that that cDNA insert encoded a full-length protein. The sequence of this cDNA insert is shown in Figure 325 and 30 is herein designated as DNA108722-2743.

Clone DNA108722-2743 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 60-62 and ending at the stop codon at nucleotide positions 1506-1508 (Figure 325). The predicted polypeptide precursor is 482 amino acids long (Figure 326). The full-length PRO7170 protein shown in Figure 326 has an estimated molecular weight of about 49,060 daltons and a pI of about 4.74. 35 Analysis of the full-length PRO7170 sequence shown in Figure 326 (SEQ ID NO:513) evidences the presence of a variety of important polypeptide domains as shown in Figure 326, wherein the locations given for those important polypeptide domains are approximate as described above. Clone DNA108722-2743 has been

deposited with ATCC on August 17, 1999 and is assigned ATCC Deposit No. 552-PTA.

An analysis of the Dayhoff database (version 35.45 SwissProt 35), using the ALIGN-2 sequence alignment analysis of the full-length sequence shown in Figure 326 (SEQ ID NO:513), evidenced sequence identity between the PRO7170 amino acid sequence and the following Dayhoff sequences: P_Y12291, I47141, D88733_1, DMC56G7_1, P_Y11606, HWP1_CANAL, HSMUC5BEX_1, HSU78550_1, HSU70136_1, and 5 SGS3_DROME.

EXAMPLE 177: Isolation of cDNA Clones Encoding Human PRO361

A consensus DNA sequence was assembled relative to other EST sequences using phrap as described in Example 1 above. This consensus sequence is herein designated DNA40654. Based on the DNA40654 10 consensus sequence, oligonucleotides were synthesized: 1) to identify by PCR a cDNA library that contained the sequence of interest, and 2) for use as probes to isolate a clone of the full-length coding sequence for PRO361.

Forward and reverse PCR primers were synthesized as follows:

<u>forward PCR primer</u>	5'-AGGGAGGATTATCCTTGACCTTGAAAGACC-3'	(SEQ ID NO:528)
<u>forward PCR primer</u>	5'-GAAGCAAGTGCCCAGCTC-3'	(SEQ ID NO:529)
<u>forward PCR primer</u>	5'-CGGGTCCCTGCTTTGG-3'	(SEQ ID NO:530)
<u>reverse PCR primer</u>	5'-CACCGTAGCTGGAGCGCACTCAC-3'	(SEQ ID NO:531)
<u>reverse PCR primer</u>	5'-AGTGTAAAGTCAAGCTCCC-3'	(SEQ ID NO:532)

Additionally, a synthetic oligonucleotide hybridization probe was constructed from the consensus 20 DNA40654 sequence which had the following nucleotide sequence
hybridization probe

5'- GCTTCCTGACACTAAGGCTGCTGCTAGTCAGAATTGCCTAAAAAGAG-3' (SEQ ID NO:533)

In order to screen several libraries for a source of a full-length clone, DNA from the libraries was screened by PCR amplification with one of the PCR primer pairs identified above. A positive library was then 25 used to isolate clones encoding the PRO361 gene using the probe oligonucleotide. RNA for construction of the cDNA libraries was isolated from human fetal kidney tissue.

DNA sequencing of the clones isolated as described above gave the full-length DNA sequence for PRO361 [herein designated as DNA45410-1250] (SEQ ID NO:514) and the derived protein sequence for PRO361.

The entire nucleotide sequence of DNA45410-1250 is shown in Figure 327 (SEQ ID NO:514). Clone 30 DNA45410-1250 contains a single open reading frame with an apparent translational initiation site at nucleotide positions 226-228 and ending at the stop codon at nucleotide positions 1519-1521 (Figure 327). The predicted polypeptide precursor is 431 amino acids long (Figure 328). The full-length PRO361 protein shown in Figure 328 has an estimated molecular weight of about 46,810 daltons and a pI of about 6.45. In addition, regions of interest including the transmembrane domain (amino acids 380-409) and sequences typical of the arginase 35 family of proteins (amino acids 3-14 and 39-57) are designated in Figure 328. Clone DNA45410-1250 has been deposited with ATCC and is assigned ATCC deposit no. ATCC 209621.

Analysis of the amino acid sequence of the full-length PRO361 polypeptide suggests that portions of it possess significant homology to the mucin and/or chitinase proteins, thereby indicating that PRO361 may be a novel mucin and/or chitinase protein.

EXAMPLE 178: Isolation of cDNA Clones Encoding a Human PRO183, PRO184, PRO185, PRO5723,

5 PRO3301 or PRO9940

DNA molecules encoding the PRO183, PRO184, PRO185, PRO5723, PRO3301 or PRO9940 polypeptides shown in the accompanying figures were obtained through GenBank.

Deposit of Material

10 The following materials have been deposited with the American Type Culture Collection, 10801 University Blvd., Manassas, VA 20110-2209, USA (ATCC):

Table 10

	<u>Material</u>	<u>ATCC Dep. No.</u>	<u>Deposit Date</u>
15	DNA45410-1250	209621	February 5, 1998
	DNA108722-2743	552-PTA	August 17, 1999
	DNA142238-2768	819-PTA	October 5, 1999
	DNA40981-1234	209439	November 7, 1997
	DNA45419-1252	209616	February 5, 1998
20	DNA44196-1353	209847	May 6, 1998
	DNA16422-1209	209929	June 2, 1998
	DNA16435-1208	209930	June 2, 1998
	DNA21624-1391	209917	June 2, 1998
	DNA23334-1392	209918	June 2, 1998
25	DNA26288-1239	209792	April 21, 1998
	DNA26843-1389	203099	August 4, 1998
	DNA26844-1394	209926	June 2, 1998
	DNA30862-1396	209920	June 2, 1998
	DNA35680-1212	209790	April 21, 1998
30	DNA40621-1440	209922	June 2, 1998
	DNA44161-1434	209907	May 27, 1998
	DNA44694-1500	203114	August 11, 1998
	DNA45495-1550	203156	August 25, 1998
	DNA47361-1154	209431	November 7, 1997
35	DNA47394-1572	203109	August 11, 1998
	DNA48320-1433	209904	May 27, 1998
	DNA48334-1435	209924	June 2, 1998
	DNA48606-1479	203040	July 1, 1998
	DNA49141-1431	203003	June 23, 1998
40	DNA49142-1430	203002	June 23, 1998
	DNA49143-1429	203013	June 23, 1998
	DNA49647-1398	209919	June 2, 1998
	DNA49819-1439	209931	June 2, 1998
	DNA49820-1427	209932	June 2, 1998
45	DNA49821-1562	209981	June 16, 1998
	DNAS2192-1369	203042	July 1, 1998
	DNAS2598-1518	203107	August 11, 1998
	DNAS3913-1490	203162	August 25, 1998

Table 10 (cont')

	DNA53978-1443	209983	June 16, 1998
	DNA53996-1442	209921	June 2, 1998
	DNA56041-1416	203012	June 23, 1998
	DNA56047-1456	209948	June 9, 1998
5	DNA56050-1455	203011	June 23, 1998
	DNA56110-1437	203113	August 11, 1998
	DNA56113-1378	203049	July 1, 1998
	DNA56410-1414	209923	June 2, 1998
	DNA56436-1448	209902	May 27, 1998
10	DNA56855-1447	203004	June 23, 1998
	DNA56859-1445	203019	June 23, 1998
	DNA56860-1510	209952	June 9, 1998
	DNA56865-1491	203022	June 23, 1998
	DNA56866-1342	203023	June 23, 1998
15	DNA56868-1209	203024	June 23, 1998
	DNA56869-1545	203161	August 25, 1998
	DNA56870-1492	209925	June 2, 1998
	DNA57033-1403	209905	May 27, 1998
	DNA57037-1444	209903	May 27, 1998
20	DNA57129-1413	209977	June 16, 1998
	DNA57690-1374	209950	June 9, 1998
	DNA57693-1424	203008	June 23, 1998
	DNA57694-1341	203017	June 23, 1998
	DNA57695-1340	203006	June 23, 1998
25	DNA57699-1412	203020	June 23, 1998
	DNA57702-1476	209951	June 9, 1998
	DNA57704-1452	209953	June 9, 1998
	DNA57708-1411	203021	June 23, 1998
	DNA57710-1451	203048	July 1, 1998
30	DNA57711-1501	203047	July 1, 1998
	DNA57827-1493	203045	July 1, 1998
	DNA57834-1339	209954	June 9, 1998
	DNA57836-1338	203025	June 23, 1998
	DNA57838-1337	203014	June 23, 1998
35	DNA57844-1410	203010	June 23, 1998
	DNA58721-1475	203110	August 11, 1998
	DNA58723-1588	203133	August 18, 1998
	DNA58737-1473	203136	August 18, 1998
	DNA58743-1609	203154	August 25, 1998
40	DNA58846-1409	209957	June 9, 1998
	DNA58848-1472	209955	June 9, 1998
	DNA58849-1494	209958	June 9, 1998
	DNA58850-1495	209956	June 9, 1998
	DNA58853-1423	203016	June 23, 1998
45	DNA58855-1422	203018	June 23, 1998
	DNA59205-1421	203009	June 23, 1998
	DNA59211-1450	209960	June 9, 1998
	DNA59213-1487	209959	June 9, 1998
	DNA59214-1449	203046	July 1, 1998
50	DNA59215-1425	209961	June 9, 1998
	DNA59220-1514	209962	June 9, 1998
	DNA59488-1603	203157	August 25, 1998
	DNA59493-1420	203050	July 1, 1998
	DNA59497-1496	209941	June 4, 1998
55	DNA59588-1571	203106	August 11, 1998

Table 10 (cont.)

	DNA59603-1419	209944	June 9, 1998
	DNA59605-1418	203005	June 23, 1998
	DNA59606-1471	209945	June 9, 1998
	DNA59607-1497	209957	June 9, 1998
5	DNA59609-1470	209963	June 9, 1998
	DNA59610-1559	209990	June 16, 1998
	DNA59612-1466	209947	June 9, 1998
	DNA59613-1417	203007	June 23, 1998
	DNA59616-1465	209991	June 16, 1998
10	DNA59619-1464	203041	July 1, 1998
	DNA59620-1463	209989	June 16, 1998
	DNA59625-1498	209992	June 17, 1998
	DNA59767-1489	203108	August 11, 1998
	DNA59776-1600	203128	August 18, 1998
15	DNA59777-1480	203111	August 11, 1998
	DNA59820-1549	203129	August 18, 1998
	DNA59827-1426	203089	August 4, 1998
	DNA59828-1608	203158	August 25, 1998
	DNA59838-1462	209976	June 16, 1998
20	DNA59839-1461	209988	June 16, 1998
	DNA59841-1460	203044	July 1, 1998
	DNA59842-1502	209982	June 16, 1998
	DNA59846-1503	209978	June 16, 1998
	DNA59847-1511	203098	August 4, 1998
25	DNA59848-1512	203088	August 4, 1998
	DNA59849-1504	209986	June 16, 1998
	DNA59853-1505	209985	June 16, 1998
	DNA59854-1459	209974	June 16, 1998
	DNA60283-1484	203043	July 1, 1998
30	DNA60615-1483	209980	June 16, 1998
	DNA60619-1482	209993	June 16, 1998
	DNA60621-1516	203091	August 4, 1998
	DNA60622-1525	203090	August 4, 1998
	DNA60625-1507	209975	June 16, 1998
35	DNA60627-1508	203092	August 4, 1998
	DNA60629-1481	209979	June 16, 1998
	DNA61755-1554	203112	August 11, 1998
	DNA61873-1574	203132	August 18, 1998
	DNA62814-1521	203093	August 4, 1998
40	DNA62872-1509	203100	August 4, 1998
	DNA62876-1517	203095	August 4, 1998
	DNA62881-1515	203096	August 4, 1998
	DNA64852-1589	203127	August 18, 1998
	DNA64884-1527	203155	August 25, 1998
45	DNA64890-1612	203131	August 18, 1998
	DNA65412-1523	203094	August 4, 1998
	DNA66308-1537	203159	August 25, 1998
	DNA66309-1538	203235	September 15, 1998
	DNA67004-1614	203115	August 11, 1998
50	DNA68869-1610	203164	August 25, 1998
	DNA68872-1620	203160	August 25, 1998
	DNA71159-1617	203135	August 18, 1998

These deposit were made under the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purpose of Patent Procedure and the Regulations thereunder (Budapest Treaty). This assures maintenance of a viable culture of the deposit for 30 years from the date of deposit. The deposits will be made available by ATCC under the terms of the Budapest Treaty, and subject to an agreement between Genentech, Inc. and ATCC, which assures permanent and unrestricted availability of the progeny of the culture of the deposit to the public upon issuance of the pertinent U.S. patent or upon laying open to the public of any U.S. or foreign patent application, whichever comes first, and assures availability of the progeny to one determined by the U.S. Commissioner of Patents and Trademarks to be entitled thereto according to 35 USC §122 and the Commissioner's rules pursuant thereto (including 37 CFR §1.14 with particular reference to 886 OG 638).

10 The assignee of the present application has agreed that if a culture of the materials on deposit should die or be lost or destroyed when cultivated under suitable conditions, the materials will be promptly replaced on notification with another of the same. Availability of the deposited material is not to be construed as a license to practice the invention in contravention of the rights granted under the authority of any government in accordance with its patent laws.

15 The foregoing written specification is considered to be sufficient to enable one skilled in the art to practice the invention. The present invention is not to be limited in scope by the construct deposited, since the deposited embodiment is intended as a single illustration of certain aspects of the invention and any constructs that are functionally equivalent are within the scope of this invention. The deposit of material herein does not constitute an admission that the written description herein contained is inadequate to enable the practice of any 20 aspect of the invention, including the best mode thereof, nor is it to be construed as limiting the scope of the claims to the specific illustrations that it represents. Indeed, various modifications of the invention in addition to those shown and described herein will become apparent to those skilled in the art from the foregoing description and fall within the scope of the appended claims.

WHAT IS CLAIMED IS:

1. Isolated nucleic acid having at least 80% sequence identity to a nucleotide sequence that encodes a polypeptide comprising an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28),
5 Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84),
10 Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure
15 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure
20 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure
25 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure
120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure
135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure
151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure
165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure
180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure
194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure
208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure
226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure
242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure
256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure
270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure

284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

2. The nucleic acid sequence of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:337).

NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

15 3. The nucleic acid of Claim 1, wherein said nucleotide sequence comprises a nucleotide sequence selected from the group consisting of the full-length coding sequence of the sequence shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure

181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

4. Isolated nucleic acid which comprises the full-length coding sequence of the DNA deposited under any ATCC accession number shown in Table 10.

25 5. A vector comprising the nucleic acid of Claim 1.

6. The vector of Claim 5 operably linked to control sequences recognized by a host cell transformed with the vector.

30 7. A host cell comprising the vector of Claim 5.

8. The host cell of Claim 7 wherein said cell is a CHO cell.

9. The host cell of Claim 7 wherein said cell is an *E. coli*.

35 10. The host cell of Claim 7 wherein said cell is a yeast cell.

11. A process for producing a PRO polypeptides comprising culturing the host cell of Claim 7 under conditions suitable for expression of said PRO polypeptide and recovering said PRO polypeptide from the cell culture.

12. Isolated PRO polypeptide having at least 80% sequence identity to an amino acid sequence selected from the group consisting of the amino acid sequence shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371)

NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 5 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) and Figure 330 (SEQ ID NO:517).

10

13. Isolated PRO polypeptide having at least 80% sequence identity to the amino acid sequence encoded by a nucleic acid molecule deposited under any ATCC accession number shown in Table 10.

15

14. A chimeric molecule comprising a polypeptide according to Claim 12 fused to a heterologous amino acid sequence.

15. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is an epitope tag sequence.

20

16. The chimeric molecule of Claim 14 wherein said heterologous amino acid sequence is a Fc region of an immunoglobulin.

17. An antibody which specifically binds to a PRO polypeptide according to Claim 12.

25

18. The antibody of Claim 17 wherein said antibody is a monoclonal antibody.

19. The antibody of Claim 17 wherein said antibody is a humanized antibody.

20. The antibody of Claim 17 wherein said antibody is an antibody fragment.

30

21. An isolated nucleic acid molecule which has at least 80% sequence identity to a nucleic acid which comprises a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 35 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46), Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50

(SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 82 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure 293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

22. An isolated nucleic acid molecule which has at least 80% sequence identity to the full-length coding sequence of a nucleotide sequence selected from the group consisting of that shown in Figure 1 (SEQ ID NO:1), Figure 3 (SEQ ID NO:5), Figure 5 (SEQ ID NO:7), Figure 8 (SEQ ID NO:13), Figure 11 (SEQ ID NO:19), Figure 14 (SEQ ID NO:22), Figure 17 (SEQ ID NO:27), Figure 19 (SEQ ID NO:29), Figure 22 (SEQ ID NO:32), Figure 24 (SEQ ID NO:35), Figure 26 (SEQ ID NO:40), Figure 29 (SEQ ID NO:46),
5 Figure 31 (SEQ ID NO:51), Figure 33 (SEQ ID NO:56), Figure 35 (SEQ ID NO:61), Figure 37 (SEQ ID NO:66), Figure 40 (SEQ ID NO:72), Figure 46 (SEQ ID NO:83), Figure 48 (SEQ ID NO:94), Figure 50 (SEQ ID NO:96), Figure 52 (SEQ ID NO:98), Figure 56 (SEQ ID NO:102), Figure 63 (SEQ ID NO:112), Figure 65 (SEQ ID NO:114), Figure 67 (SEQ ID NO:116), Figure 69 (SEQ ID NO:118), Figure 71 (SEQ ID NO:123), Figure 73 (SEQ ID NO:128), Figure 75 (SEQ ID NO:134), Figure 78 (SEQ ID NO:137), Figure 10 (SEQ ID NO:145), Figure 84 (SEQ ID NO:147), Figure 87 (SEQ ID NO:150), Figure 89 (SEQ ID NO:152), Figure 92 (SEQ ID NO:155), Figure 94 (SEQ ID NO:157), Figure 96 (SEQ ID NO:159), Figure 98 (SEQ ID NO:164), Figure 100 (SEQ ID NO:166), Figure 102 (SEQ ID NO:168), Figure 104 (SEQ ID NO:170), Figure 108 (SEQ ID NO:174), Figure 110 (SEQ ID NO:176), Figure 112 (SEQ ID NO:178), Figure 114 (SEQ ID NO:180), Figure 116 (SEQ ID NO:182), Figure 119 (SEQ ID NO:188), Figure 121 (SEQ ID 15 NO:193), Figure 124 (SEQ ID NO:196), Figure 126 (SEQ ID NO:198), Figure 128 (SEQ ID NO:200), Figure 130 (SEQ ID NO:202), Figure 132 (SEQ ID NO:204), Figure 134 (SEQ ID NO:206), Figure 136 (SEQ ID NO:208), Figure 138 (SEQ ID NO:210), Figure 140 (SEQ ID NO:212), Figure 143 (SEQ ID NO:215), Figure 146 (SEQ ID NO:218), Figure 148 (SEQ ID NO:220), Figure 150 (SEQ ID NO:222), Figure 152 (SEQ ID NO:224), Figure 154 (SEQ ID NO:226), Figure 156 (SEQ ID NO:228), Figure 158 (SEQ ID NO:230), Figure 20 160 (SEQ ID NO:235), Figure 162 (SEQ ID NO:240), Figure 164 (SEQ ID NO:245), Figure 166 (SEQ ID NO:247), Figure 168 (SEQ ID NO:249), Figure 170 (SEQ ID NO:252), Figure 173 (SEQ ID NO:255), Figure 175 (SEQ ID NO:257), Figure 177 (SEQ ID NO:259), Figure 179 (SEQ ID NO:261), Figure 181 (SEQ ID NO:263), Figure 183 (SEQ ID NO:265), Figure 185 (SEQ ID NO:267), Figure 187 (SEQ ID NO:269), Figure 189 (SEQ ID NO:271), Figure 191 (SEQ ID NO:273), Figure 193 (SEQ ID NO:275), Figure 195 (SEQ ID 25 NO:277), Figure 197 (SEQ ID NO:280), Figure 199 (SEQ ID NO:282), Figure 201 (SEQ ID NO:284), Figure 203 (SEQ ID NO:286), Figure 205 (SEQ ID NO:288), Figure 207 (SEQ ID NO:290), Figure 209 (SEQ ID NO:292), Figure 211 (SEQ ID NO:294), Figure 213 (SEQ ID NO:296), Figure 215 (SEQ ID NO:298), Figure 217 (SEQ ID NO:300), Figure 219 (SEQ ID NO:302), Figure 225 (SEQ ID NO:308), Figure 227 (SEQ ID NO:313), Figure 229 (SEQ ID NO:318), Figure 232 (SEQ ID NO:325), Figure 234 (SEQ ID NO:333), Figure 30 237 (SEQ ID NO:339), Figure 239 (SEQ ID NO:344), Figure 241 (SEQ ID NO:346), Figure 243 (SEQ ID NO:348), Figure 245 (SEQ ID NO:350), Figure 247 (SEQ ID NO:352), Figure 249 (SEQ ID NO:354), Figure 251 (SEQ ID NO:356), Figure 253 (SEQ ID NO:358), Figure 255 (SEQ ID NO:360), Figure 257 (SEQ ID NO:362), Figure 259 (SEQ ID NO:364), Figure 261 (SEQ ID NO:366), Figure 263 (SEQ ID NO:368), Figure 265 (SEQ ID NO:370), Figure 267 (SEQ ID NO:372), Figure 269 (SEQ ID NO:374), Figure 271 (SEQ ID 35 NO:376), Figure 273 (SEQ ID NO:378), Figure 275 (SEQ ID NO:380), Figure 277 (SEQ ID NO:386), Figure 279 (SEQ ID NO:388), Figure 281 (SEQ ID NO:393), Figure 283 (SEQ ID NO:398), Figure 285 (SEQ ID NO:400), Figure 287 (SEQ ID NO:402), Figure 289 (SEQ ID NO:407), Figure 291 (SEQ ID NO:409), Figure

293 (SEQ ID NO:411), Figure 295 (SEQ ID NO:413), Figure 297 (SEQ ID NO:415), Figure 299 (SEQ ID NO:417), Figure 301 (SEQ ID NO:419), Figure 303 (SEQ ID NO:421), Figure 305 (SEQ ID NO:423), Figure 307 (SEQ ID NO:494), Figure 309 (SEQ ID NO:496), Figure 311 (SEQ ID NO:498), Figure 313 (SEQ ID NO:500), Figure 315 (SEQ ID NO:502), Figure 317 (SEQ ID NO:504), Figure 319 (SEQ ID NO:506), Figure 321 (SEQ ID NO:508), Figure 323 (SEQ ID NO:510), Figure 325 (SEQ ID NO:512), Figure 327 (SEQ ID NO:514) and Figure 329 (SEQ ID NO:516).

5 23. An isolated extracellular domain of of PRO polypeptide.

10 24. An isolated PRO polypeptide lacking its associated signal peptide.

25. An isolated polypeptide having at least about 80% amino acid sequence identity to an extracellular domain of of PRO polypeptide.

15 26. An isolated polypeptide having at least about 80% amino acid sequence identity to a PRO polypeptide lacking its associated signal peptide.

27. Isolated nucleic acid having at least 80% nucleic acid sequence identity to:

(a) a nucleotide sequence encoding the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure

20 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33),

Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41

(SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID

25 115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure

93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure

30 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure

125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure

139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure

155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure

169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

(b) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID

NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

(c) a nucleotide sequence encoding an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure

90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

28. An isolated polypeptide having at least 80% amino acid sequence identity to:
35 (a) the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36),

Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:509)

NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide;

NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), with its associated signal peptide; or

5 (c) an extracellular domain of the polypeptide shown in Figure 2 (SEQ ID NO:2), Figure 4 (SEQ ID NO:6), Figure 6 (SEQ ID NO:8), Figure 9 (SEQ ID NO:14), Figure 12 (SEQ ID NO:20), Figure 15 (SEQ ID NO:23), Figure 18 (SEQ ID NO:28), Figure 20 (SEQ ID NO:30), Figure 23 (SEQ ID NO:33), Figure 25 (SEQ ID NO:36), Figure 27 (SEQ ID NO:41), Figure 30 (SEQ ID NO:47), Figure 32 (SEQ ID NO:52), Figure 34 (SEQ ID NO:57), Figure 36 (SEQ ID NO:62), Figure 38 (SEQ ID NO:67), Figure 41 (SEQ ID NO:73), Figure 47 (SEQ ID NO:84), Figure 49 (SEQ ID NO:95), Figure 51 (SEQ ID NO:97), Figure 53 (SEQ ID NO:99), Figure 57 (SEQ ID NO:103), Figure 64 (SEQ ID NO:113), Figure 66 (SEQ ID NO:115), Figure 68 (SEQ ID NO:117), Figure 70 (SEQ ID NO:119), Figure 72 (SEQ ID NO:124), Figure 74 (SEQ ID NO:129), Figure 76 (SEQ ID NO:135), Figure 79 (SEQ ID NO:138), Figure 83 (SEQ ID NO:146), Figure 85 (SEQ ID NO:148), Figure 88 (SEQ ID NO:151), Figure 90 (SEQ ID NO:153), Figure 93 (SEQ ID NO:156), Figure 95 (SEQ ID NO:158), Figure 97 (SEQ ID NO:160), Figure 99 (SEQ ID NO:165), Figure 101 (SEQ ID NO:167), Figure 103 (SEQ ID NO:169), Figure 105 (SEQ ID NO:171), Figure 109 (SEQ ID NO:175), Figure 111 (SEQ ID NO:177), Figure 113 (SEQ ID NO:179), Figure 115 (SEQ ID NO:181), Figure 20 117 (SEQ ID NO:183), Figure 120 (SEQ ID NO:189), Figure 122 (SEQ ID NO:194), Figure 125 (SEQ ID NO:197), Figure 127 (SEQ ID NO:199), Figure 129 (SEQ ID NO:201), Figure 131 (SEQ ID NO:203), Figure 133 (SEQ ID NO:205), Figure 135 (SEQ ID NO:207), Figure 137 (SEQ ID NO:209), Figure 139 (SEQ ID NO:211), Figure 141 (SEQ ID NO:213), Figure 144 (SEQ ID NO:216), Figure 147 (SEQ ID NO:219), Figure 149 (SEQ ID NO:221), Figure 151 (SEQ ID NO:223), Figure 153 (SEQ ID NO:225), Figure 155 (SEQ ID NO:227), Figure 157 (SEQ ID NO:229), Figure 159 (SEQ ID NO:231), Figure 161 (SEQ ID NO:236), Figure 163 (SEQ ID NO:241), Figure 165 (SEQ ID NO:246), Figure 167 (SEQ ID NO:248), Figure 169 (SEQ ID NO:250), Figure 171 (SEQ ID NO:253), Figure 174 (SEQ ID NO:256), Figure 176 (SEQ ID NO:258), Figure 178 (SEQ ID NO:260), Figure 180 (SEQ ID NO:262), Figure 182 (SEQ ID NO:264), Figure 184 (SEQ ID NO:266), Figure 186 (SEQ ID NO:268), Figure 188 (SEQ ID NO:270), Figure 190 (SEQ ID NO:272), Figure 192 (SEQ ID NO:274), Figure 194 (SEQ ID NO:276), Figure 196 (SEQ ID NO:278), Figure 198 (SEQ ID NO:281), Figure 200 (SEQ ID NO:283), Figure 202 (SEQ ID NO:285), Figure 204 (SEQ ID NO:287), Figure 206 (SEQ ID NO:289), Figure 208 (SEQ ID NO:291), Figure 210 (SEQ ID NO:293), Figure 212 (SEQ ID NO:295), Figure 214 (SEQ ID NO:297), Figure 216 (SEQ ID NO:299), Figure 218 (SEQ ID NO:301), Figure 220 (SEQ ID NO:303), Figure 226 (SEQ ID NO:309), Figure 228 (SEQ ID NO:314), Figure 230 (SEQ ID NO:319), Figure 233 (SEQ ID NO:326), Figure 235 (SEQ ID NO:334), Figure 238 (SEQ ID NO:340), Figure 240 (SEQ ID NO:345), Figure 242 (SEQ ID NO:347), Figure 244 (SEQ ID NO:349), Figure 246 (SEQ ID NO:351), Figure 248 (SEQ ID NO:353), Figure 250 (SEQ ID NO:355), Figure 252 (SEQ ID NO:357), Figure 35

254 (SEQ ID NO:359), Figure 256 (SEQ ID NO:361), Figure 258 (SEQ ID NO:363), Figure 260 (SEQ ID NO:365), Figure 262 (SEQ ID NO:367), Figure 264 (SEQ ID NO:369), Figure 266 (SEQ ID NO:371), Figure 268 (SEQ ID NO:373), Figure 270 (SEQ ID NO:375), Figure 272 (SEQ ID NO:377), Figure 274 (SEQ ID NO:379), Figure 276 (SEQ ID NO:381), Figure 278 (SEQ ID NO:387), Figure 280 (SEQ ID NO:389), Figure 282 (SEQ ID NO:394), Figure 284 (SEQ ID NO:399), Figure 286 (SEQ ID NO:401), Figure 288 (SEQ ID NO:403), Figure 290 (SEQ ID NO:408), Figure 292 (SEQ ID NO:410), Figure 294 (SEQ ID NO:412), Figure 296 (SEQ ID NO:414), Figure 298 (SEQ ID NO:416), Figure 300 (SEQ ID NO:418), Figure 302 (SEQ ID NO:420), Figure 304 (SEQ ID NO:422), Figure 306 (SEQ ID NO:424), Figure 308 (SEQ ID NO:495), Figure 310 (SEQ ID NO:497), Figure 312 (SEQ ID NO:499), Figure 314 (SEQ ID NO:501), Figure 316 (SEQ ID NO:503), Figure 318 (SEQ ID NO:505), Figure 320 (SEQ ID NO:507), Figure 322 (SEQ ID NO:509), Figure 324 (SEQ ID NO:511), Figure 326 (SEQ ID NO:513), Figure 328 (SEQ ID NO:515) or Figure 330 (SEQ ID NO:517), lacking its associated signal peptide.

29. A method of detecting a PRO943 polypeptide in a sample suspected of containing a PRO943 polypeptide, said method comprising contacting said sample with a PRO183, PRO184 or PRO185 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO943 polypeptide in said sample.

30. The method according to Claim 29, wherein said sample comprises cells suspected of expressing said PRO943 polypeptide.

31. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is labeled with a detectable label.

32. The method according to Claim 29, wherein said PRO183, PRO184 or PRO185 polypeptide is attached to a solid support.

33. A method of detecting a PRO183, PRO184 or PRO185 polypeptide in a sample suspected of containing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said sample with a PRO943 polypeptide and determining the formation of a PRO943/PRO183, PRO184 or PRO185 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO183, PRO184 or PRO185 polypeptide in said sample.

34. The method according to Claim 33, wherein said sample comprises cells suspected of expressing said PRO183, PRO184 or PRO185 polypeptide.

35. The method according to Claim 33, wherein said PRO943 polypeptide is labeled with a detectable label.

36. The method according to Claim 33, wherein said PRO943 polypeptide is attached to a solid support.

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37. A method of detecting a PRO331 polypeptide in a sample suspected of containing a PRO331 polypeptide, said method comprising contacting said sample with a PRO1133 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO331 polypeptide in said sample.

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38. The method according to Claim 37, wherein said sample comprises cells suspected of expressing said PRO331 polypeptide.

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39. The method according to Claim 37, wherein said PRO1133 polypeptide is labeled with a detectable label.

40. The method according to Claim 37, wherein said PRO1133 polypeptide is attached to a solid support.

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41. A method of detecting a PRO1133 polypeptide in a sample suspected of containing a PRO1133 polypeptide, said method comprising contacting said sample with a PRO331 polypeptide and determining the formation of a PRO331/PRO1133 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1133 polypeptide in said sample.

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42. The method according to Claim 41, wherein said sample comprises cells suspected of expressing said PRO1133 polypeptide.

43. The method according to Claim 41, wherein said PRO331 polypeptide is labeled with a detectable label.

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44. The method according to Claim 41, wherein said PRO331 polypeptide is attached to a solid support.

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45. A method of detecting a PRO363 or PRO5723 polypeptide in a sample suspected of containing a PRO363 or PRO5723 polypeptide, said method comprising contacting said sample with a PRO1387 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO363

or PRO5723 polypeptide in said sample.

46. The method according to Claim 45, wherein said sample comprises cells suspected of expressing said PRO363 or PRO5723 polypeptide.

5 47. The method according to Claim 45, wherein said PRO1387 polypeptide is labeled with a detectable label.

48. The method according to Claim 45, wherein said PRO1387 polypeptide is attached to a solid support.

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49. A method of detecting a PRO1387 polypeptide in a sample suspected of containing a PRO1387 polypeptide, said method comprising contacting said sample with a PRO363 or PRO5723 polypeptide and determining the formation of a PRO363 or PRO5723/PRO1387 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1387 polypeptide in said sample.

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50. The method according to Claim 49, wherein said sample comprises cells suspected of expressing said PRO1387 polypeptide.

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51. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is labeled with a detectable label.

52. The method according to Claim 49, wherein said PRO363 or PRO5723 polypeptide is attached to a solid support.

25

53. A method of detecting a PRO1114 polypeptide in a sample suspected of containing a PRO1114 polypeptide, said method comprising contacting said sample with a PRO3301 or PRO9940 polypeptide and determining the formation of a PRO1114/PRO3301 or PRO9940 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1114 polypeptide in said sample.

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54. The method according to Claim 53, wherein said sample comprises cells suspected of expressing said PRO1114 polypeptide.

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55. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is labeled with a detectable label.

56. The method according to Claim 53, wherein said PRO3301 or PRO9940 polypeptide is attached to a solid support.

57. A method of detecting a PRO3301 or PRO9940 polypeptide in a sample suspected of containing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said sample with a PRO1114 polypeptide and determining the formation of a PRO3301 or PRO9940/PRO1114 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO3301 or PRO9940 polypeptide in said sample.

10 58. The method according to Claim 57, wherein said sample comprises cells suspected of expressing said PRO3301 or PRO9940 polypeptide.

59. The method according to Claim 57, wherein said PRO1114 polypeptide is labeled with a detectable label.

15 60. The method according to Claim 57, wherein said PRO1114 polypeptide is attached to a solid support.

20 61. A method of detecting a PRO1181 polypeptide in a sample suspected of containing a PRO1181 polypeptide, said method comprising contacting said sample with a PRO7170, PRO361 or PRO846 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO1181 polypeptide in said sample.

25 62. The method according to Claim 61, wherein said sample comprises cells suspected of expressing said PRO1181 polypeptide.

63. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is labeled with a detectable label.

30 64. The method according to Claim 61, wherein said PRO7170, PRO361 or PRO846 polypeptide is attached to a solid support.

35 65. A method of detecting a PRO7170, PRO361 or PRO846 polypeptide in a sample suspected of containing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said sample with a PRO1181 polypeptide and determining the formation of a PRO1181/PRO7170, PRO361 or PRO846 polypeptide conjugate in said sample, wherein the formation of said conjugate is indicative of the presence of a PRO7170, PRO361 or PRO846 polypeptide in said sample.

66. The method according to Claim 65, wherein said sample comprises cells suspected of expressing said PRO7170, PRO361 or PRO846 polypeptide.

67. The method according to Claim 65, wherein said PRO1181 polypeptide is labeled with a detectable label.

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68. The method according to Claim 65, wherein said PRO1181 polypeptide is attached to a solid support.

69. A method of linking a bioactive molecule to a cell expressing a PRO943 polypeptide, said 10 method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

70. The method according to Claim 69, wherein said bioactive molecule is a toxin, a radiolabel 15 or an antibody.

71. The method according to Claim 69, wherein said bioactive molecule causes the death of said cell.

72. A method of linking a bioactive molecule to a cell expressing a PRO183, PRO184 or PRO185 20 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide that is bound to said bioactive molecule and allowing said PRO943 and PRO183, PRO184 or PRO185 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

73. The method according to Claim 72, wherein said bioactive molecule is a toxin, a radiolabel 25 or an antibody.

74. The method according to Claim 73, wherein said bioactive molecule causes the death of said cell.

75. A method of linking a bioactive molecule to a cell expressing a PRO331 polypeptide, said 30 method comprising contacting said cell with a PRO1133 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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76. The method according to Claim 75, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

77. The method according to Claim 75, wherein said bioactive molecule causes the death of said cell.

78. A method of linking a bioactive molecule to a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide that is bound to said bioactive molecule and allowing said PRO331 and PRO1133 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

79. The method according to Claim 78, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

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80. The method according to Claim 78, wherein said bioactive molecule causes the death of said cell.

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81. A method of linking a bioactive molecule to a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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82. The method according to Claim 81, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

83. The method according to Claim 81, wherein said bioactive molecule causes the death of said cell.

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84. A method of linking a bioactive molecule to a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide that is bound to said bioactive molecule and allowing said PRO1387 and PRO363 or PRO5723 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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85. The method according to Claim 84, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

86. The method according to Claim 84, wherein said bioactive molecule causes the death of said cell.

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87. A method of linking a bioactive molecule to a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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88. The method according to Claim 87, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

89. The method according to Claim 87, wherein said bioactive molecule causes the death of said cell.

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90. A method of linking a bioactive molecule to a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide that is bound to said bioactive molecule and allowing said PRO1114 and PRO3301 or PRO9940 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

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91. The method according to Claim 90, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

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92. The method according to Claim 90, wherein said bioactive molecule causes the death of said cell.

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93. A method of linking a bioactive molecule to a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

94. The method according to Claim 93, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

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95. The method according to Claim 93, wherein said bioactive molecule causes the death of said cell.

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96. A method of linking a bioactive molecule to a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide that is bound to said bioactive molecule and allowing said PRO1181 and PRO7170, PRO361 or PRO846 polypeptides to bind to one another, thereby linking said bioactive molecules to said cell.

97. The method according to Claim 96, wherein said bioactive molecule is a toxin, a radiolabel or an antibody.

98. The method according to Claim 96, wherein said bioactive molecule causes the death of said cell.

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99. A method of modulating at least one biological activity of a cell expressing a PRO943 polypeptide, said method comprising contacting said cell with a PRO183, PRO184 or PRO185 polypeptide or an anti-PRO943 antibody, whereby said PRO183, PRO184 or PRO185 polypeptide or said anti-PRO943 antibody binds to said PRO943 polypeptide, thereby modulating at least one biological activity of said cell.

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100. The method according to Claim 99, wherein said cell is killed.

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101. A method of modulating at least one biological activity of a cell expressing a PRO183, PRO184 or PRO185 polypeptide, said method comprising contacting said cell with a PRO943 polypeptide or an anti-PRO183, anti-PRO184 or anti-PRO185 antibody, whereby said PRO943 polypeptide or said anti-PRO183, anti-PRO184 or anti-PRO185 antibody binds to said PRO183, PRO184 or PRO185 polypeptide, thereby modulating at least one biological activity of said cell.

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102. The method according to Claim 101, wherein said cell is killed.

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103. A method of modulating at least one biological activity of a cell expressing a PRO331 polypeptide, said method comprising contacting said cell with a PRO1133 polypeptide or an anti-PRO331 antibody, whereby said PRO1133 polypeptide or said anti-PRO331 antibody binds to said PRO331 polypeptide, thereby modulating at least one biological activity of said cell.

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104. The method according to Claim 103, wherein said cell is killed.

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105. A method of modulating at least one biological activity of a cell expressing a PRO1133 polypeptide, said method comprising contacting said cell with a PRO331 polypeptide or an anti-PRO1133 antibody, whereby said PRO331 polypeptide or said anti-PRO1133 antibody binds to said PRO1133 polypeptide, thereby modulating at least one biological activity of said cell.

106. The method according to Claim 105, wherein said cell is killed.

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107. A method of modulating at least one biological activity of a cell expressing a PRO1387 polypeptide, said method comprising contacting said cell with a PRO363 or PRO5723 polypeptide or an anti-PRO1387 antibody, whereby said PRO363 or PRO5723 polypeptide or said anti-PRO1387 antibody binds to said PRO1387 polypeptide, thereby modulating at least one biological activity of said cell.

5 108. The method according to Claim 107, wherein said cell is killed.

109. A method of modulating at least one biological activity of a cell expressing a PRO363 or PRO5723 polypeptide, said method comprising contacting said cell with a PRO1387 polypeptide or an anti-PRO363 or anti-PRO5723 antibody, whereby said PRO1387 polypeptide or said anti-PRO363 or anti-PRO5723 antibody binds to said PRO363 or PRO5723 polypeptide, thereby modulating at least one biological activity of said cell.

110. The method according to Claim 109, wherein said cell is killed.

15 111. A method of modulating at least one biological activity of a cell expressing a PRO1114 polypeptide, said method comprising contacting said cell with a PRO3301 or PRO9940 polypeptide or an anti-PRO1114 antibody, whereby said PRO3301 or PRO9940 polypeptide or said anti-PRO1114 antibody binds to said PRO1114 polypeptide, thereby modulating at least one biological activity of said cell.

20 112. The method according to Claim 111, wherein said cell is killed.

113. A method of modulating at least one biological activity of a cell expressing a PRO3301 or PRO9940 polypeptide, said method comprising contacting said cell with a PRO1114 polypeptide or an anti-PRO3301 or anti-PRO9940 antibody, whereby said PRO1114 polypeptide or said anti-PRO3301 or anti-PRO9940 antibody binds to said PRO3301 or PRO9940 polypeptide, thereby modulating at least one biological activity of said cell.

114. The method according to Claim 113, wherein said cell is killed.

30 115. A method of modulating at least one biological activity of a cell expressing a PRO1181 polypeptide, said method comprising contacting said cell with a PRO7170, PRO361 or PRO846 polypeptide or an anti-PRO1181 antibody, whereby said PRO7170, PRO361 or PRO846 polypeptide or said anti-PRO1181 antibody binds to said PRO1181 polypeptide, thereby modulating at least one biological activity of said cell.

35 116. The method according to Claim 115, wherein said cell is killed.

117. A method of modulating at least one biological activity of a cell expressing a PRO7170, PRO361 or PRO846 polypeptide, said method comprising contacting said cell with a PRO1181 polypeptide or an anti-PRO7170, anti-PRO361 or anti-PRO846 antibody, whereby said PRO1181 polypeptide or said anti-PRO7170, anti-PRO361 or anti-PRO846 antibody binds to said PRO7170, PRO361 or PRO846 polypeptide, thereby modulating at least one biological activity of said cell.

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118. The method according to Claim 117, wherein said cell is killed.

FIGURE 1

CGGACGCGTGGGTGCGAGGCAGAGGTGACCGGGGACCGAGCATTGAGATCTGCTCGGTAGA
CCTGGTGCACCACCACCA**TG**TTGGCTGCAAGGCTGGTGTCTCCGGACACTACCTCTAGG
GTTTCCACCCAGCTTCACCAAGGCCTCCCTGGTGAAGAATTCCATCACGAAGAATCA
ATGGCTGTTAACACCTAGCAGGGAATATGCCACAAAACAAGAATTGGGATCCGGCGTGGGA
GAACCTGGCCAAGAACTCAAAGAGGCAGCATTGGAACCATCGATGGAAAAAATTAAAATT
GATCAGATGGGAAGATGGTTGTTGCTGGAGGGCTGCTGTTGGCTTGGAGCATTGTGCTA
CTATGGCTTGGACTGTCTAATGAGATTGGAGCTATTGAAAAGGCTGTAATTGGCCTCAGT
ATGTCAAGGATAGAATTCAATTCCACCTATATGACTTAGCAGGGAGTATTGGTTAACAGCT
TTGTCTGCCATAGCAATCAGCAGAACGCCTGTTCTCATGAACCTCATGATGAGAGGCTCTG
GGTGACAATTGGTGTGACCTTGCAGCCATGGTGGAGCTGGAATGCTGGTACGATCAATAC
CATATGACCAGAGCCCAGGCCAAAGCATTGCTGGTGCCTACATTCTGGTGTGATGGGT
GCAGTGGTGGCTCCTGACAATATTAGGGGTCCTCTCATCAGAGCTGCATGGTACAC
AGCTGGCATTGGGGAGGCCTCCACTGTGGCCATGTGCGCCAGTAAAAGTTCTGA
ACATGGGTGCACCCCTGGGAGTGGGCTGGTCTCGTCTTGTGTCCTCATTGGGATCTATG
TTTCTTCCACCTACCACCGTGGCTGGTGCCTACTCTTACTCAGTGGCAATGTACGGTGGATT
AGTTCTTTCAAGCATGTTCTCTGTATGATAACCCAGAAAGTAATCAAGCGTCAGAAGTAT
CACCAATGTATGGAGTTCAAAATATGATCCCATTAACTCGATGCTGAGTATCTACATGGAT
ACATTAATATATTATGCGAGTTGCAACTATGCTGGCAACTGGAGGCAACAGAAAAGAA**TG**
AAGTGACTCAGCTCTGGCTCTGCTACATCAAATATCTGTTAATGGGGCAGATATGC
ATTAATAGTTGTACAAGCAGCTTCGTTGAAGTTAGAAGATAAGAAACATGTCATCATA
TTTAAATGTCCGGTAATGTGATGCCTCAGGTCTGCCTTTCTGGAGAATAATGCAGT
AATCCTCTCCAAATAAGCACACACATTTCATTCTCATGTTGAGTGAATTAAATGTT
TTGGTGAATGTGAAAACATAAGTTGTGATGAGAATGTAAGTCTTTCTACTTTAAA
TTTAGTAGGTTCACTGAGTAACAAAATTAGCAAACCTGTGTTGCATATTGGAGT
GCAGAAATTGTAATTAAATGTCTAAGTGTGATTGGAGCTTGGTAAAGGGACAGAGAG
GAGTCACCTGCAGTCTTGTGTTAAATACTTAGAACTTAGCACTTGTGTTATTGATTA
GTGAGGAGCAGTAAGAAACATCTGGTATTGGAAACAAGTGGTCATTGTTACATTCA
GCTGAACCTAACAAACTGTTCATCCTGAAACAGGCACAGGTGATGCATTCTCCTGCTGTG
CTTCTCAGTGCTCTTCCAATATAGATGTGGTCATGTTGACTTGTACAGAATGTTAAC
ATACAGAGAATCCTGATGGAATTATATATGTGTTTACTTTGAATGTTACAAAAGGAA
ATAACTTAAACTATTCTCAAGAGAAAATTCAAAGCATGAAATATGTTGCTTTCCAG
AATACAAACAGTATACTCATG

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FIGURE 2

MLAARLVCLRTLPSRVFHPAFTKASPVVKNSITKNQWLLTPSREYATKTRIGIRRGRTGQEL
KEAALEPSMEKIFKIDQMGRWFVAGGAAVGLGALCYGLGLSNEIGAIEKAVIWPQYVKDRI
HSTYMYLAGSIGLTALSAIAISRTPVLMNFMMRGSWVTIGVTFAAMVGAGMLVRSIPYDQSP
GPKHLAWLLHSGVMGAVVAPLTILGGPLLIRAAWYTAGIVGGLSTVAMCAPSEKFLNMGAPL
GVGLGLVFVSSLGSMFLPPTTVAGATLYSVAMYGGVLFSMFLLYDTQKVIKRAEVSPMYGV
QKYDPINSMLSIIYMDTLNIFMRVATMLATGGNRKK

FIGURE 3

GAAGGCTGCCTCGCTGGTCCGAATTGGTGGCGCCACGTCCGCCGCTCTCCGCCTCTGCAT
CGCGGCTTCGGCGGCTTCCACCTAGACACCTAACAGTCGGAGGCCGCGTCGTGAGGG
GGTCGGCACGGGGAGTCGGCGGTCTTGTGCATCTGGCTACCTGTGGGTGAAAGATGTGG
ACATGGAGACTGGTCAGGAGCATCCGGCGATCACGCGCTATTGGTTCGCCGCCACCGTC
GCCGTGCCCTGGTCGGCAAACCTGGCCTCATCAGCCGCCACCTCTCCCTGGCCCGA
AGCCTCCTTATCGCTTCAGATTGGAGGCCAATCACTGCCACCTTTATTTCCTGTGG
GTCCAGGAACGGATTCTTATTGGTCAATTATTTCTTATATCAGTATTCTACGCGA
CTTGAAACAGGAGCTTGTGATGGGAGGCCAGCAGACTATTATTCATGCTCCTCTTAACTG
GATTTGATCGTGTGATTACTGGCTTAGCAATGGATATGCAGTGCTGATGATTCCCTGATCA
TGTCACTTTATGTCTGGGCCAGCTGAACAGAGACATGATTGATCATTTGGTTGGA
ACACGATTTAAGGCTGCTATTACCTGGGTTATCCTGGATTCAACTATATCATCGGAGG
CTCGGTAAATCAATGAGCTTGGAAATCTGGTTGGACATCTTATTTCCTAATGTTCA
GATAAAAATGGACTTGGAGGAAGAAATTTCATCCACACCTCAGTTTGTAACCGCTGG
CTGCCAGTAGGAGAGGAGGAGTACAGGATTGGTGTGCCCTGCTAGCATGAGGCAGC
TGCTGATCAGAATGGCGGAGGCCAGACACAACGGGCTTCGACTGGAGACC
AGTGAAGGGCGGCCCTCGGGCAGCCGCTCTCAAGCCACATTCTCCAGTGCTGGGTG
CACTTAACAACGCTGCTCTGGCTAACACTGTTGGACCTGACCCACACTGAATGTAGTCTTC
AGTACGAGACAAAGTTCTTAAATCCGAAGAAAAAAATAAGTGTCCACAAGTTACGAT
TCTCATTCAAGCTTACTGCTGTGAAGAACAAATACCAACTGTGCAAATTGCAAACACTGAC
TACATTTTTGGTGTCTCTCTCTCCCTTCCGCTGTGAATAATTGGGTTTAGCGGGTCT
AATCTGCTGGCATTGAGCTGGGCTGGTCACCAACCCCTCCAAAAGGACCTATCTCT
TCTGCACACATGCCTCTCCCACCTTCCCAACCCCCACATTGCAACTAGAAAAAGTTG
CCCATAAAATTGCTCTGCCCTGACAGGTTCTGTTATTGACTTTGCCAAGGCTGGC
ACAACAATCATATTACGTTATTTCCCTTTGGTGGCAGAACTGTTACCAATAGGGGAG
AAGACAGCCACGGATGAAGCGTTCTCAGCTTTGAAATTGCTCGACTGACATCCGTT
AACCGTTGCCACTCTCAGATATTTTATAAAAAAAAGTACCAACTGAGTTCATGAGGCCA
CAGATTGGTATAATGAGATACAGGGTTGGTGTGGTTCTGAGCTAAGTGA
TCAAGACTGTAGTGGAGTTGAGCTAACATGGGTTAGGTTAAACCATGGGGATGCACCCC
TTTGCCTTCATATGTAGCCCTACTGGCTTGTGAGCTGGAGTAGTTGGTTGCTTGTG
TAGGAGGATCCAGATCATGTTGGCTACAGGGAGATGCTCTTGTGAGAGGCTGGCATG
ATTCCCATTCAATCTCATTCTGGATATGTGTTCATGAGTAAGGAGGAGAGACCCCTATA
CGCTATTAAATGTCACTTTTGCCCTATCCCCGTTTTGGTCATGTTCAATTAAATTG
GAGGAAGGCGCAGCTCCTCTGCACGTAGATCATTTAAAGCTAATGTAAGCACATCTA
AGGAAATAACATGTTAAGGTTGAAATGGCTTAAAGCTTGGTTGAGGGTGTGTTA
TTTGAGTCATGAAATGTCACAGCTGTGAATCAGACCAGCTTAAACCAACACCTTTT
TCGTAGGTGGCTTTCTCATCAGAGCTGGCTCATACCAAAATAAGTTTTGAAGGCCA
TGGCTTTCACACAGTTATTATGACGTTATCTGAAAGCAGACTGTTAGGAGCACT
ATTGAGTGGCTGTACACTTGGAGGCAACTAAAAGGCTCAAACGTTGATCAGTTCTT
TTCAGGAAACATTGCTCTAACAGTATGACTATTCTCCCACTCTAAACAGTGTGAT
GTGTGTTATCTTAGGAAATGAGAGTTGGCAAACAACTTCTCATTTGAATAGAGTTGTG
TACTTCTCCATATTAAATTATGATAAAATAGGTGGGAGAGTCTGAAACCTTAACGTC
TGTGTTGTTGTCATCTGTCACAAATAAGTTACTGTAAGGAGGCCATTACT
CCAATTATGTCACGCTACACTCATTGACAGGGCGTGGAGACTCATTGATGATAAGAATA
TTCTGACAGTGAGTGACCCGGAGTCTGGTGTACCCCTTACCAAGTCAGCTGCCCTGCGAG
CAGTCATTCTAAAGGTTACAAGTATTAGAACTTTCAAGTTGATCAGGCAAAATGTC
ATGAAGTTATTCTCTTAAACATGGTAGGAAGCTGATGACGTTATTGATTTGCTGGATT
ATGTTCTGGAATAATTACAAAACAAGCTATTGAGTTGACTTGACAAGGCAAAACA
TGACAGTGGATTCTCTTACAAATGGAAAAAAATCCTTATTGTATAAAGGACTTCCC
TTTGTAAACTAATCCTTTATTGGTAAAATTGTAATGCAACTTG

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FIGURE 4

MSDIGDWFRSIPAITRYWFAATVAVPLVGKGLISPAYLFLWPEAFLYRFQIWRPITATFYF
PVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNWICIVITGLAMDMQLLMIP
LIMSVLYVWAQLNNDMIVSFWFGRFKACYLPWVILGFNYIIGGSVINEIGNLVGHLYFFL
MFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGGRHNWGQGFRL
GDQ

Transmembrane domain:

amino acids 98-116, 152-172

N-myristoylation site.

amino acids 89-95, 168-174, 176-182, 215-221, 221-227, 237-243

Glycosaminoglycan attachment site.

amino acids 218-222

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FIGURE 5

GGGGCCGCGGTCTAGGGCGGCTACGTGTGTCATAGCGACCATTTGCATTAACGGTTG
GTAGCTCTATCCTGGGGGCTGAGCGACTGCGGGCCAGCTCTTCCCCTACTCCCTCTCGGCT
CCTTGTGGCCAAAGGCCTAACCGGGTCCGGCGGTCTGGCCTAGGGATCTCCCCGTTGCC
CCTTGGGGCGGGATGGCTGCGGAAGAAGAAGACGAGGTGGAGTGGTAGTGGAGAGCATCG
CGGGGTTCCCTGCGAGGCCAGACTGGTCATCCCCATCTTGGACTTTGTGGAACAGAAATGT
GAAGTTAAC TGCAAAGGAGGGCATGTGATAACTCCAGGAAGCCCAGAGCCGGTATTTGGT
GGCCTGTGTTCCCTGTTTGATGATGAAGAAGAAAGCAAATTGACCTATA CAGAGATT
ATCAGGAATACAAAGAACTAGTGAAAAGCTGTTAGAAGGTACCTCAAAGAAATTGGAATT
AATGAAGATCAATTCAAGAACGCATGCACCTCTCCTCTGCAAAGACCCATACATCACAGGC
CATTTGCAACCTGTGTTGGCAGCAGAAGATTACTATCTTAAAGCAATGATGGTCCAGA
AAAACATTGAAATGCAGCTGCAAGCCATCGAATAATTCAAGAGAGAAATGGTGTATTACCT
GACTGCTTAACCGATGGCTCTGATGTGGCAGTGACCTTGAACACGAAGAGATGAAAATCCT
GAGGGAAGTTCTTAGAAAATCAAAAGAGGAATATGACCAGGAAGAAGAAAGGAAGAGGAAAA
AACAGTTATCAGAGGCTAAACAGAACAGAGCCCACAGTCGATCCAGTGAAGCTGCAATAATG
AATAATTCCAAGGGGATGGTGAACATTGACACACCCACCCCTCAGAAGTTAAATGCATT
TGCTAATCAGTCATAGAACCTTGGGAAGAAAAGTGGAAAGGTCTGAAACTTCCCTCC
CACAAAAGGCCTGAAGATTCTGGCTTAGAGCATGCGAGCATTGAAGGACCAATAGCAAAC
TTATCAGTACTTGGAACAGAACAGAACACTATCTCAAGCAGAACAGAGA
TAAGTTGATGTCCATGAGAAAGGATATGAGGACTAACAGATACAAAATATGGAGCAGAAAG
GAAAACCCACTGGGGAGGTAGAGGAATGACAGAGAAACCAAGAAATGACAGCAGAGGAGAAG
CAAACATTACTAAAGAGGAGATTGCTGCAGAGAAACTCAAAGAAGAAGTTATTAATAAGTA
ATAATTAAGAACATTAACAAAATGGAAGTTCAAATTGTCTAAAATAATTATTTAGTC
CTTACACTG

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FIGURE 6

MAAEEEDEVWVVEVSIAGFLRGPDWSIPILDFVEQKCEVNCKGGHVITPGSPEPVILVACVP
LVFDDEEESKLTYTEIHQEYKELVEKLLEGYLKEIGINEDQFQEACTSPLAKTHSQAILQP
VLAADFTIFKAMMVQKNIEMQLQAIRIIQERNGVLPDCLTDGSDVVSDEHEEMKILREVL
RKSKEEYDQEEERKRKKQLSEAKTEEPTVHSSEAAIMNNSQGDGEHFAHPPSEVKMHFANQS
IEPLGRKVERSETSSLPKGLKIPGLEHASIEGPIANLSVLGTEELRQREHYLKQKRDKLM
MRKDMRTKQIQNMEQKGKPTGEVEEMTEKPEMTAEEKQTLLKRRLLAEKLKEEVINK

N-glycosylation sites.

amino acids 224-228, 246-250, 285-289

N-myristoylation site.

amino acids 273-279

Amidation site.

amino acids 252-256

Cytosolic fatty-acid binding proteins.

amino acids 78-108

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FIGURE 7

GGGCACAGCACATGTGAAGTTTGATGATGAAGAAGAAAGCAAATTGACCTATACAGAGAT
TCATCAGGAATAACAAAGAACTAGTTGAAAAGCTGTTAGAAGGTTACCTCAAAGAAATTGGAA
TTAATGAAGATCAATTCAAGAACGCATGCACCTCTCCTCTGCAAAGACCCATACATCACAG
GCCATTTTGCAACCTGTGTTGGCAGCAGAAGATTACTATCTTAAAGCAATGATGGTCC
AGAAAAACATTGAAATGCAGCTGCAAGCCATTGAAATAATTCAAGAGAGAAATGGTGTATTA
CCTGACTGCTTAACCGATGGCTCTGATGTGGTCAGTGACCTGAACACGAAGAGATGAAAAT
CCTGAGGGAAGTTCTTAGAAATCAAAGAGGAATATGACCAGGAA

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FIGURE 8

GC GTGGTTTGTCTGCAATAGGCGGCTTAGAGGGAGGGCTTTGCCCTATACCTACTG
TAGCTTCTCACGTATGGACCTAAAGGCTACTGCTGCTACTACGGGCTAGACAGTTACTG
TCTCAGCTCTAGGATGTGCGTTCTTCACTAGAAGCTCTGAGGGAGGTAATTAAAAAC
AGTGGAA**ATG**AAAAACAGTGTAGTCATCCTGTAATATGCTCCTGTCAACAATGTATAC
ATTCCTGCTAGGTGCCATATTGCTTAAGCTCAAGTGCATCTTACTAGTGAAGTATT
CTGCCAATGAAGAAAACAAGTATGATTATCTTCCAACACTACTGTGAATGTGCTCAGAACCTG
GTGAAGCTAGTTCTGTGCTGTGTCATTCTGTGTTATAAAAGAAAGATCATCAAAGTAG
AAATTGAAATATGCTCCTGGAGGAATTCTCTGATTTCATGAAGTGGTCCATTCTGCCT
TTCTTATTCTGGATAACTTGATTGCTTCTATGCTCTATCTCAACCAGCCATG
GCTGTTATCTCTCAAATTAGCATTATAACACAGCTCTCTATTAGGATAGTGTGAA
GAGGCGTCTAAACTGGATCCAGTGGGCTTCCCTGACTTATTTGTCTATTGTGCT
TGACTGCCGGACTAAAACCTTACAGCACAACTGGCAGGACGTGGATTTCATCACGATGCC
TTTTCAGCCCTTCCAATTCTGCCTCTTCAGAAGTGAGTGTCCCAGAAAAGACAATTG
TACAGCAAAGGAATGGACTTTCTGAAGCTAAATGGAACACCACAGCCAGAGTTTCAGTC
ACATCCGTCTGGCATGGCCATGTTCTTATTAGTCCAGTGTGTTATTCTCAATGGCT
AATATCTATAATGAAAAGATACTGAAGGAGGGAAACAGCTACTGAAAGCATCTTCATACA
GAACAGCAAACCTATTCTGGCATTCTGTTATGGGCTGACTCTGGCCTTCAGAGGA
GTAACCGTGATCAGATTAAGAACTGTGGATTTTATGGCCACAGTCATTTCAGTAGCC
CTTATTGTAACTGCATTCCAGGGCCTTCACTGCTTCTGATTTCTGAAAGCCCCATCAGTCCTCTCTATA
TCTTGACTTCAGGCCCTCCCTGAAATTCTTCTGAAAGCCTTCACTGCTTCTCTATA
TTTATTATAATGCCAGCAAGCTCAAGTTCCGGAAATACGCACCTAGGCAAGAAAGGATCCG
AGATCTAAGTGGCAATCTTGGAGCGTCCAGTGGGATGGAGAAGAACTAGAAAAGACTTA
CCAAACCAAGAGTGAGTCAGATGAAGATACTTC**TAAC**TGGTACCCACATAGTTGCA
GCTCTCTGAACCTTATTTCACATTTCAGTGTGTTGAATATTATCTTCACTTTGATA
AACCAGAAATGTTCTAAATCTTAAATATTCTGATATATCTAGCTACTCCCTAAATGGTT
CCATCCAAGGCTTAGAGTACCCAAAGGCTAAGAAATTCTAAAGAACTGATACAGGAGTAACA
ATATGAAGAATTCTAAATATCTCAGTACTTGATAAAATCAGAAAGTTATATGTGAGATTAT
TTCTGAGCTTCAAGCTCCAAAAACTGTAATAATCATGTTAGCTATAGCTTGTATAT
ACACATAGAGATCAATTGCCAAATATTACAATCATGTAGTTCTAGTTACATGCCAAAGT
CTTCCCTTTAACATTATAAAAGCTAGGTTGTCTCTGAATTGGAGGCCCTAGAGATAGT
CATTGCAAGTAAAGAGCAACGGGACCCCTTCTAAAACGTTGGTGAAGGACCTAAATAC
CTGGCCATACCATAGATTGGGATGATGTTAGCTGTGCTAAATATTGCTGAAGAAGCAGT
TTCTCAGACACAACATCTCAGAATTAAATTAGAAATTCTAGGGAAATTGGATTTGT
AATAATCTTGTGTTAACATTGGTCCCTAGTCACCATAGTTACCACTTGTATTAA
AGTCATTAAACAAGCCACGGTGGGCTTTCTCCTCAGTTGAGGGAGAAAATCTGAT
GTCATTACTCTGAATTATTACATTGGAGAATAAGAGGGCTTTCTGCTCAGAATCATA
AATTCAAGCTGTGACTATTGTATATCTTCAAGAGTTGAATGCTGGCTTCAGAATCATA
CAGATTGTCAGTGAAGCTGATGCCCTAGGAACCTTAAAGGGATCTTCAAAAGGATCACTT
AGCAAACACATGTTGACTTTAAGTGTATGAATATTAACTCTAAAATAGAAAGACC
AGTAATATAAGTCACTTACAGTGTACTTCACACTTAAAGTCATGGTATTTCATG
GTATTTGCATGCAGGCCAGTTAAGTGTAGATAGAGAAGTCAGGTGATAGATGATATTAA
AAATTAGCAAACAAAAGTGACTTGCTCAGGGTCTGAGCTGGGTGATGATAGAAGAGTGGG
CTTAACTGGCAGGCCGTATGTTACAGACTACCATACTGTAATATGAGCTTATGGTGT
CATTCTCAGAAACTTACACATTCTGCTCTCCTTCTCCTAAGTTCATGCAGATGAATATA
AGGAATATAACTATTATAATTCAATTGTGATATCCACAATAATGACTGGCAAGAATTG
GTGGAAATTGTAAATTAAAATAATTAAACCT

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FIGURE 9

MEKQCCSHPVICSLSTMYTFLLGAIFIALSSSRILLVKYSANEENKYDYLPTTVNVCSELVK
LVFCVLVSFCVIKKDHQSRLNKYASWKEFSDFMKWSIPAFLYFLDNLIVFYVLSYLPAMAV
IFSNFSIITTALLFRIVLKRRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFF
SPSNCLLFRSECPRKDNCATAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISSLANI
YNEKILKEGNQLTESIFIQNSKLYFFGILFNGLQLQRSNRDQIKNCGFFYGHSAFSVALI
FVTAFQGLSVAFILKFLDNMFHVLMAQVTTVIITTVSVLVFDFRPSLEFFLEAPSVLSSIFI
YNASKPQVPEYAPRQERIRDLSGNLWERSSGDGEELERLTKPKSDESDEDTF

Transmembrane domains:

amino acids 16-36 (type II), 50-74, 147-168, 229-250, 271-293,
298-318, 328-368

N-glycosylation sites.

amino acids 128-132, 204-208, 218-222, 374-378

Glycosaminoglycan attachment site.

amino acids 402-406

N-myristoylation sites.

amino acids 257-263, 275-281, 280-286, 284-290, 317-323

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FIGURE 10

CGTGCCTGCGCAATGGGTGTCGGGTCCGCTTTCCCAATCCGGACGTAATCGTGGTTTG
TTCTGCAATAGGCGGCTTAGAGGGAGGGCTTTGCCTATACCTACTGTAGCTTCTCCAC
GTATGGACCTAAAGGCTACTGCTGCTACTACGGGGCTAGACAGTTACTGTCTAGCTCTAG
GATGTGCGTTCTTCCACTAGAACGCTTCTGAGGGAGGTAAATTAAAAAACAGTGGAAATGGAA
AAACAGTGCTGTAGTCATCCTGTAATATGCTCCTGTCAACAAATGTATACATTCCGTAGG
TGCCATATTCAATTGCTTTAAGCTCAAGTCGATCTTACTAGTGAAGTATTCTGCCAATGAAG
AAAACAAGTATGATTATCTTCAAACACTGTGAATGTGTGCTCAGAACTGGTGAAGCTAGTT
TTCTGTGTGCTTGTGTCATTCTGTGTTATAAGAAAGATCATCAAAGTAGAAATTGAAATA
TGCTTCCTGGAAGGAATTCTCTGATTTCATGAAGTGGTCCATTCCCTGCCTTCTTATTCC
TGGATAACTGATTGTCTTCTATGTCCTGTCCATCTCAACCAGCCATGGCTGTTATCTC
TCAAATTAGCATTATAACAAACAGCTCTTCTATTCAAGGATAGTGTGAAGAGGCGTCAA
CTGGATCCAGTGGCTTCCCTCCTGACTTTATTGTGCTATTGTGGCCTGACTGCCGGGA
CTAAAACTTA

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FIGURE 11

CGGACGCGTGGCGGACGCGTGGCGGACGCGTGGGGCGGGCTTGGCTAGCGCGCGGGCC
GTGGCTAAGGCTGCTACGAAGCGAGCTGGGAGGAGCAGCGGCCTGCCGGCAGAGGAGCAT
CCCGTCTACCAGGTCCAAGCGCGTGGCCCGCGGGCTATGCCAAAGGAGAAGGCAGCGAG
AGCGGCTCCGCGGGCTGCTACCCACCAGCATCCTCAAAGCACTGAACGCCCGGCCA
GGTGAAGAAAGAACGAAAAAGAAGAAACAACAGTTGCTGTTGACAACAAGCTTGCTATG
CACTGGGGAGCCCTTACCAAGGTGACGGGCTGTGCCCTGGGTTCTCCTCAGATCTAC
CTATTGGATGTGGCTCAGGTGGCCCTTCTGCCTCCATCATCCTGTTGTGGGCCAGC
CTGGGATGCCATCACAGACCCCTGGTGGGCCTCTGCATCAGCAAATCCCCCTGGACCTGCC
TGGGTCGCCCTATGCCCTGGATCATCTCTCCACGCCCTGGCGTCAATTGCCTACTCCTC
ATCTGGTTCGTGCCCACCTCCCACACGCCAGACCTATTGGTACCTGCTTTCTATTGCCT
CTTGAAACAATGGTCACGTGTTCCATGTCCTACTCGGCCTCACCAGTTGTCATCAGCA
ACCGAGCAGACTGAGCGGGATTCTGCCACCGCCTATGGATGACTGTGGAAGTGTGGCAC
AGTGCTGGGCACGGCAGTCCAGGGACAAATCGTGGCCAAGCAGACACGCCCTTGTTCAGG
ACTTCAATAGCTCTACAGTAGCTTACAAAGTGCCAACATACACATGGCACCACCTCACAC
AGGGAAACGCAAAGGCATACCTGCTGGCAGCGGGGTATGTCTGTATCTATATAATCTG
TGCTGTATCCTGATCTGGCGTGCAGGAGCAGAGAGAACCTATGAAGGCCAGCAGTCTG
AGCCAATGCCCTACTTCCGGGCCTACGGCTGGTATGAGCCACGCCCATACATCAAACCTT
ATTACTGGCTTCCCTTCACCTCCTGGCTTCATGCTGGTGGAGGGAACTTGTCTTGT
TTGCACCTACACCTGGCTTCCGCAATGAATTCCAGAATCTACTCCTGGCCATCATGCTCT
CGGCCACTTAACCATCCCACCTGGCAGTGGTCTTGACCCGGTTGGCAAGAAGACAGCT
GTATATGTTGGGATCTCATCAGCAGTGCCTTCTCATCTGGTGGCCCTATGGAGAGTAA
CCTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCCTTAC
TACCTGGTCCATGCTGCCTGATGTCATTGACGACTCCATCTGAAGCAGCCCCACTCCAT
GGAACCGAGCCCATTCTCTTCTATGTTCTTACCAAGTTGCCCTGGAGTGT
ACTGGGCATTCTACCCCTCAGTCTGGACTTGCAGGGTACCAAGACCCGGCTGCTCGCAGC
CGGAACGTGTCAGTTACACTGAACATGCTCGTACCATGGCTCCATAGTTCTCATCCTG
CTGGGCCTGCTGCTCTCAAAATGTACCCATTGATGAGGAGAGGCAGGAGAATAAGAA
GCCCTGCAGGCAGTGGGAGGCCAGCAGCTGGCTGCTCAGAAACAGACTCCACAG
AGCTGGCTAGCATCCTTAGGGCCGCCAGTTGCCGAAGCCACCATGCGAGGCCACAG
AAGGGATCAGGACCTGCTGCCGGCTTGCTGAGCAGCTGGACTGCAGGTGCTAGGAAGGGAA
CTGAAGACTCAAGGAGGTGGCCAGGACACTTGCTGTGCTACTGTGGGGCCGGCTGCTCTG
TGGCCTCTGCCTCCCTCTGCCTGCTGTGGGGCCAAGGCCCTGGGGCTGCCACTGTGAATA
TGCCAAGGACTGATGGGCCTAGCCGAAACACTAATGTAGAAACCTTTTACAGAGCC
TAATTAATAACTTAATGACTGTGTCATAGCAATGTGTGTATGTATGTGAGCTA
TTAATGTTATTAATTCATAAAAGCTGGAAAGC

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FIGURE 12

MWLRWALS LPPSSCLWAEPGMPSQT PWWASASANPPGPAWVALCPGSSSPRPWPSLPTSSSG
SCPTSHTARPIGTCFSIASLKQWSRVSMFPTRLSPCSSATEQTERDSATAYRMTVEVLGTVL
GTAIQGQIVGQADTPCFQDFNSSTVASQSANHTHGTTSHRETQKAYLLAAGVIVCIYIICAV
ILILGVREQREPYEAQQSEPIAYFRGLRLVMSHGPYIKLITGFLFTSLAFMLVEGNFVLFCT
YTIGFRNEFQNLLLAIMLSATLTIPIWQWFLTRFGKKTAVYVGIISSAVPFLILVALMESNLI
ITYAVAVAAGISVAAFLLPWSMLPDVIDDFHLKQPHFHGT EPIFFSFYVFFTKFASGVSLG
ISTLSLDFAGYQTRGCSQPERVKFTLNMLVTMAPIVLILLGLLFKMYPIDEERRRQNKKAL
QALRDEASSSGCSETDSTELASIL

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FIGURE 13

GGGAAACGAAAAGGCATACTGCTGGCAGCGGGGTCATTGTCTGTATCTATATAATCTGT
GCTGTCATCCTGATCCTGGCGTGCAGGAGCAGAGAGAACCTATGAAGCCCAGCAGTCTGA
GCCAATCGCCTACTTCCGGGCCTACGGCTGGTCATGAGCCACGGCCCACATCAAACCTTA
TTACTGGCTCCTCTTCACCTCCTTGGCTTCATGCTGGTGGAGGGAACTTGTCTGTT
TGCACCTACACCTTGGCTTCCGCAATGAATTCCAGAACATCTACTCCTGGCCATCATGCTCTC
GGCCACTTTAACCATCCCCATCTGGCAGTGGTTCTGACCCGGTTGGCAAGAACAGCTG
TATATGTTGGGATCTCATCAGCAGTGCCATTCTCATCTTGGTGGCCCTCATGGAGAGTAAC
CTCATCATTACATATGCGGTAGCTGTGGCAGCTGGCATCAGTGTGGCAGCTGCCTTCTTACT
ACCCTGGTCATGCTGCCTGATGTCATTGACGACTTCCATCTGAAGCAGCCCCACTCCATG
GAACCGAGCCCCAT

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FIGURE 14

GGGGCTCGCGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGGATTACAAAAGGTGCAGGT
ATGAGCAGGTCTGAAGACTAACATTGTGAAGTTGTAAAACAGAAAACCTGTTAGAAATGT
GGTGGTTTCAGCAAGGCCTCAGTTCTTCAGCCCTTGTAAATTGGACATCTGCTGCT
TTCATATTTCATACATTACTGCAGTAACACTCCACCATATAGACCCGGCTTACCTTATAT
CAGTGACACTGGTACAGTAGCTCCAGAAAATGCTTATTGGGGCAATGCTAAATATTGCGG
CAGTTTATGCATTGCTACCATTATGTTGTTATAAGCAAGTTCATGCTCTGAGTCCTGAA
GAGAACGTTATCATCAAATTAAACAAGGCTGGCCTGTACTTGGAAATACTGAGTTGTTAGG
ACTTTCTATTGTGGCAAACCTCCAGAAAACAACCCCTTTGCTGCACATGTAAGTGGAGCTG
TGCTTACCTTGGTATGGGCTCATTATATGTTGTTCAGACCATCCTTCCTACCAAATG
CAGCCCCAAATCCATGGCAAACAAGTCTCTGGATCAGACTGTTGGTTATCTGGTGTGG
AGTAAGTGCACTTAGCATGCTGACTTGCTCATCAGTTTGCACAGTGGCAATTGGGACTG
ATTAGAACAGAAACTCCATTGGAACCCCGAGGACAAAGGTTATGTGCTTCACATGATCACT
ACTGCAGCAGAATGGTCTATGTCATTTCCTTGGTTTCTGACTTACATTGTA
TTTCAGAAAATTCTTACGGTGGAAAGCCAATTACATGGATTAACCCCTATGACACTG
CACCTTGCCTATTAACAATGAACGAACACGGCTACTTCCAGAGATATTTGATGAAAGGAT
AAAATATTCTGTAATGATTATGATTCTCAGGGATTGGGAAAGGTTCACAGAAGTTGCTTA
TTCTTCTGAAATTTCACCCTTAATCAAGGCTGACAGTAACACTGATGAATGCTGATA
ATCAGGAAACATGAAAGCATTGATAGATTATTCTAAAGGATATCATCAAGAAGACTA
TTAAAAACACCTATGCCTATACTTTTATCTCAGAAAATAAGTCAAAAGACTATG

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FIGURE 15

MWWFQQGLSFLPSALVIWTSAAFIFSYITAVTLHHIDPALPYISDTGTVAPEKCLFGAMLNI
AAVLCIATIYVRYKQVHALSPEENVIIKLNKAGLVLGILSCLGLSIVANFQKTLFAAHVSG
AVLTFGMGSLYMFVQTILSYQMOPKIHGKQVFWIRLLVIWCGVSALSMLTCSVLHSGNFG
TDLEQKLHWNPEDKGYVLHMITTAAEWSMSFSFFGFFLTYIRDFQKISLRVEANLHGLTLYD
TAPCPINNERTRLLSRDI

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FIGURE 16

CGGACGCTTGGGCNGGCCAGCGGCCAGCGCTAGTCGGTCTGGTAAGTGCCTGATGCCGAGT
TCCGTCTCTCGGGTCTTTCCTGGTCCCAGGCAAAGCGGAGCGGAGATCCTCAAACGGCCTA
GTGCTTCGCGCTTCCGGAGAAAATCAGCGGTCTAATTAATTCTCTGGTTGTTGAAGCAGT
TACCAAGAATCTTCAACCCTTCCCACAAAAGCTAATTGAGTACACGTTCTGTTGAGTACA
CGTTCCCTGTTGATTACAAAAGGTGCAGGTATGAGCAGGTCTGAAGACTAACATTGTGAA
GTTGTAAAACAGAAAACCTGTTAGAAATGTGGTGGTTTCAGCAAGGCCTCAGTTCCCTCCT
TCAGCCCTTGTAAATTGGACATCTGCTGCTTCATATTTCATACATTACTGCAGTAACACT
CCACCATATAGACCCGGCTTACCTATATCAGTGACACTGGTACAGTANC

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FIGURE 17

CCACCGCGTCCGCCGCCGCTGCGTCCGGAGTGCAAGTGAGCTCTCGGCTGCCCGCGGG
CCGGGGTGCGGAGCCGACATCGCCCGCTCTCGGCCTCCTCTGGTCTCGCCGGCTGCAC
CTTCGCCTTGTACTTGCTGTCACGCGACTGCCCGGGCGGAGACTGGGCTCCACCGAGG
AGGCTGGAGGCAGGTGCGTGTGGTCCCTCGACCTGGCAGAGCTGCGGGAGCTCTGAG
GTCCTTCGAGAGTACCGGAAGGAGCACCAGGCCTACGTGTTCTGCTCTGCGGCGCTA
CCTCTACAAACAGGGTTGCCATCCCCGCTCCAGCTTCTGAATGTTTAGCTGGTGCT
TGTTGGCCATGGCTGGGCTCTGCTGTGTTGACCTCGGTGGTGCCACATGC
TGCTACCTGCTCTCCAGTATTTGGCAAACAGTTGGTGGTGCCTACTTCCTGATAAAGT
GGCCCTGCTGCAGAGAAAGGTGGAGGAGAACAGAAACAGCTGTTTTCTTATTGTTT
TGAGACTTTCCCCATGACACCAAACGGTTCTGAACCTCTGGCCCCAATTCTGAACATT
CCCATCGTGCAGTTCTTCTCAGTTCTATCGGTTGATCCCATAATTCTGTGT
GCAGACAGGGTCCATCCTGTCAACCTAACCTCTGGATGCTTTCTCCTGGACACTG
TCTTAAGCTGTTGCCATTGCCATGGCATTAATTCTGGAACCCCTATTAAAAAATT
AGTCAGAAACATCTGCAATTGAATGAAACAAGTACTGCTAATCATATAACAGTAGAAAAGA
CACATTGACTGGATTTCTGTTGCCACATCCCTGGACTCAGTTGCTTATTGTGAATGGA
TGTGGCCTCTAAAGCCCTCATTGTTGATTGCCCTATAGGTGATGTGGACACTGTG
CATCAATGTGCAGTGTCTTCAGAAAGGACACTCTGCTCTGAAGGTGTATTACATCAGGT
TTTCAAACCAGCCCTGGTGTAGCAGACACTGCAACAGATGCCCTAGAAAATGCTGTTGT
GGCCGGGCGCGGTGGCTACGCCGTAAATCCCAGCACCTTGGAGGCCAGGCGGTGATTG
ACAAGGTCAAGGAGTTCAAGACCAGCCTGCCAAGATGGTAAATCCTGTCTAATAAAAAT
ACAAAAATTAGCCAGGCAGGTGGCAGGCACCTGTAATCCCAGCTACTCGGGAGGCTGAGGC
AGGAGAATTGCTTGAACCAAGGTGGCAGAGGTTGCAAGTAAGCCAAGATCACACCACTGCACT
CCAGCCTGGGTGATAGAGTGAAGACACTGTCTTGAC

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FIGURE 18

MRPLLGLLLVFAGCTFALYLLSTRLPRGRRLGSTEEAGGRSLWFPSDLAELRELSEVLREYR
KEHQAYVFLFCGAYLYKQGFAIPGSSFLNVLAGALFGPWLGLLLCCVLTSGATCCYLLSS
IFGKQLVVSYFPDKVALLQRKVEENRNSLFFFLLFLRLFPMTPNWFNLNSAPILNIPIVQFF
FSVLIGLIPYNFICVQTGSILSTLTSLDALFSWDTVKLLAIAMVALIPGTLIKKFSQKHLQ
LNETSTANHIHSRKDT

Important features:

Signal peptide:

amino acids 1-17

Transmembrane domains:

amino acids 101-123, 189-211

N-glycosylation sites.

amino acids 172-176, 250-254

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 240-244, 261-265

N-myristoylation site.

amino acids 13-19, 104-110, 115-121, 204-210

Amidation site.

amino acids 27-31

Prokaryotic membrane lipoprotein lipid attachment site.

amino acids 4-15

Protein splicing proteins.

amino acids 25-31

Sugar transport proteins.

amino acids 162-172

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FIGURE 19

CCGAGGCAGGGAGGAGCCGAGGGGGCGCGAGCCCCCATGAATCATTGAGTCATCATT
CCAGTTCTCAGCCGCTCAGTTGATCAAGGGACACGTGGTTCCGAAGCTGCCAGCTCAGAA
TAGGAAAATAACTGGGATTTATATTGAAGACATGGATCTGCTGCCAACGAGATCAGCA
TTTATGACAAAACCTTCAGAGACTGTTGATTGGTGAGACAGACCCGGCATCAGTGTGGCATG
TCAGAGAAGGCAATTGAAAAATTATCAGACAGCTGCTGGAAAAGAATGAACCTCAGAGACC
CCCCCGCAGTATCCTCTCCTTATAGTTGTATAAGGTTCTCGAACCTGGGATTAATCT
TGCTCACTGCCACTTTGTGATTCAACCTTCAGCCCATTAGCACCTGAGCCAGTGCTTCT
GGAGCTCACACCTGGCGCTCACTCATCCATCACATTAGGCTGATGTCCTGCCATTGCCAA
GAAGTACATGTCAAGAAAATAAGGGAGTTCTCTGCATGGGGGTGATGAAGACAGACCCCTTC
CAGACTTGACCCCTGGTGGACAAACGACTGTGAGCAGAATGAGTCAGAGCCCATTCTGCC
AACTGCACTGGCTGTGCCAGAAAACACCTGAAGGTGATGCTCTGGAAGACGCCCAAGGAA
ATTGAGAGGGCTCCATCCACTGGTGATCAAGACGGAAAGCCCTGTTGGAGGAAGAGATTG
AGCATTGGCGCTGCTTCCCTGAGCGGTGGTCCCATTCCCTATCCATGGAGGAGACCTCTGAA
CAGATCACAAATGTTACGTGAGCTTCTGTTCACTCACCTGCCATTCCAAAAGATG
CCTCTTAAACAAGTGCCTTCTCACCCAGAACCTGTTGTGGGAGTAAGATGCATAAG
ATGCCTGACCTATTTATCATTGGCAGCGGTGAGGCCATGTTGCAGCTCATCCCTCCCTCCA
GTGCCGAAGACATTGTCAGTCTGTGGCCATGCCAATAGAGCCAGGGATATCGCTATGTCG
ACACCAACCACTGGAAGGTCTACGTTAGCCAGAGGGTCCAGCCTTGGTCATCTGCGAT
GGAACCGCTTCTCAGAACTGTAGGAAATAGAACTGTCACAGGAACAGCTCCAGAGCCGA
AAACCAGGTTGAAAGGGAAAATAAAACAAAACGATGAAACTGCAAAAA

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FIGURE 20

MDLAANEISIYDKLSETVDLVRQTGHQCGMSEKAIEKFIRQLLEKNEPQRPPPQYPLLIVVY
KVLATLGLILLTAYFVIQPFSPLAPEPVLSGAHTWRSЛИHHIRLMSLPIAKKYMSENKGVPL
HGGDEDRPFPDFDPWWTNDCQESEPIPANCTGCAQKHLKVMLLEDAPRKFERLHPLVIKT
GKPLLEEEIQHFLCQYPEATEGFSEGFFAKWWRCFPERWFPPYPWRRPLNRSQMLRELFPV
FTHLPFPKDASLNKCSFLHPEPVVGSKMHKMPDLFIIGSGEAMLQLIIPPFQCRRHCQSVAMP
IEPGDIGYVDTTHWKVYVIARGVQPLVICDGTAFSEL

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FIGURE 21

CCACGGTGTCCGTTCTCGCCCGGCGCAGCTGTCCCCGAGGCAGGAGGCCGAGGGCG
CGAGCCCCGATGAATCATTGAGTCATTCAGTTCTCAGCCGTTCAGTTGTGATC
AAGGGACACGTGGTTCCGAACGCCAGCTCAGAATAGGAAAATAACTTGGGATTTATATT
GGAAGACATGGATCTTGCTGCCAACGAGATCAGCATTATGACAAACTTCAGAGACTGTTG
ATTGGTGAGACAGACCGGCCATCACTGAGTCAGAGAAGGCAATTGAAAAATTATC
AGACAGCTGCTGGAAAAGAACCTCAGAGACCCCCCGCAGTATCCTCTCCTTATAGT
TGTGTATAAGGTTCTCGAACCTGGGATTAATCTGCTCACTGCCTACTTGTGATTCAAC
CTTCAGCCCATTAGCACCTGAGCCAGTGCTTGTGGAGCTCAC

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FIGURE 22

CCACCGCGTCCGCCAACCGCTCCGGCTGAACACCTCTTGGAGTCAGCCACTGATGAGG
 CAGGGTCCCCACTTGAGCTGCAGCAGCTGCAGCAGCTGCAGAGCGCTGCTCCTGGCTGGTG
 CCACTGGTGCACGCTGCTAGACCGTGCCTATGAGCGCTGGGGCTGCAGTGGGACTGCC
 CTCCCTGCCACCCACCAATGGCAGCCCCACCTTCTTGAAGACTTCCAGGCTTTGTGCCA
 CACCCGAATGGCAGCTTCATCGACAAACAGGTACAGCCAACC**ATG**CCCAGTTGAAATG
 GACACGTATGCTAAGAGCCACGACCTTATGTCAGGTTCTGGAATGCTGTATGACATGCT
 TATGAGCAGTGGCAGCGGCCAGTGGAGCGCGCCAGAGTCGTCGGGCCTTCCAGGAGC
 TGGTGTGAAACCTGCGCAGAGGCAGGGCTGCTGACTACCGCAGTGCAG
 AAGCAGCAGCAACCGCAGCACTCCATGGGCCCTGCTGACTGGGGGCGCTGTGGCAGCAGT
 CGCAGCCCAGTGGGGCTGGCAGGGACACTCCATCCCCCGCTGGAAACTGTCCA
 GCGCCGAGACATATTACGCATCGCTGAAGCTGGTGCCTACACTTCGACCCCTCAC
 CTGGAAGCCAGCGCTCTCGAGACAATCTGGTGGAGGTTCCCTGACACCCACCGAGGAGC
 CTCACTGCCCTCTGGCAGTGACCAAAGAGGCCAAAGTGGAGCAGCCCCACCGAGTTGCTGCAGG
 AGGACCAGCTGGCGAGGACGAGCTGGCTGAGCTGGAGACCCGATGGAGGGCAGCAGAACTG
 GATGAGCAGCGTGGAGAGCTGGTGTGTCGGCGAGTGCCAGCTGGTACGGTAGTGGCGT
 GGTCCCAGGGCTGCTGGAGGTACCCACACAGAATGTATACTCTACGATGGCAGCACTGAGC
 GCGTGGAAACCGAGGGCATCGGCTATGATTCCGGCAGCCACTGGCCAGCTGCGTGAG
 GTCCACCTGCGCGTTCAACCTGCGCCGTTCACTGGGACTCTTATCGATCAGGC
 CAACTACTTCTCAACTTCCATGCAAGGTGGCAGCAGCCCCAGTCTCATCTCCTAGCCAGA
 CTCCGAGACCCCAGCTGGCCCCATCCCCACCCATACCCAGGTACGGAACCAAGGGTACTCG
 TGGCTCTGCGCTACGGCCCCCTCTAAGGCTACCTAACGAGCCGCTCCCCCAGGAGAT
 GCTGCGTGCCTCAGGCTTACCCAGAAATGGGTACAGCGTGAGATATCAAACCTCGAGTACT
 TGATGCAACTAACACCAATTGCGGGCGGACCTACAATGACCTGTCTCAGTACCCCTGTGTT
 CCCGGGTCTGCAAGGACTACGTGTCCCCAACCTGGACCTCAGCAACCCAGCCGCTTCCG
 GGACCTGCTAAGCCATCGGTGGTGAACCCCAAGCATGCCAGCTCGTGAGGGAGAAGT
 ATGAAAGCTTGGAGGACCCAGCAGGGACATTGACAAGTCCACTATGGCACCCACTACTCC
 AATGCAAGCAGCGTGTGCACTACCTCATCCGCGTGGAGCCCTTCACCTCCCTGACGTCCA
 GCTGCAAAGTGGCGCTTGTACTGCTCCGACGGCAGTTCAACTCGGTGGCGGAGCCTGGC
 AGGCACGCCCTGGAGAGCCCTGCCATGTGAAGGAGCTCATCCCGGAATTCTACTTCT
 GACTTCCCTGGAGAACCCAGAACGGTTTGACCTGGGCTGTCTCCAGCTGACCAACGAGAAGGT
 AGGCATGTGGTGTACCCCCGGGGCAGCTCTTGAGGACTTCATCCAGCAGCACCGCC
 AGGCTCTGGAGTGGAGTATGTGTCTGCAACACCTACAGGAGGGATGACCTCATTTGGC
 TACAAGCAGCGGGGGCCAGCCGGAGGGCCCTCAATGTCCTCTATTACTGCAACCTATGA
 GGGGCTGAGACCTGGGACCATGTGACAGATGAGCGGGAAAGGGCTGGGAGGGCATTA
 TCAGCAACTTGGGCAAGACTCCCTGTCAGCTGCTGAAGGAGCCACATCCAACCTGGCTCTCA
 GCTGAGGAAGCAGCCCATGCCCTGCAAGGGCTGGACACTAACACTCCATCTCAGGCTGGCA
 CCTGGACGAACCTCAAGGCTTCTCGCAGAGGTGACTGTGAGTGCCAGTGGCTGCTGGGCA
 CCCACAGCTGGTGTGCCCTATGACCGAACATAAGCAACTACTTCAGCTCAGCAAAGACCC
 ACCATGGGCAAGCCACAAGACGCACTGCTGAGTGGCCGTGGGTGCCAGGCAGTGGTGT
 GAGTGGACAAGCACTGGCAGTGGCCGGATGAAAGCTGCTATTCAAGCGGTGGCCACTGGG
 ATGGCAGCCCTGCGGGTGAECTGCAACTACCCCTGGCAAGCTGTTGAGGCCAGCTCAGCTGCCAC
 CTTGATGTAGTAACCTGCCCTGCACTGGACACCTGTGGCATCTACCTCATCTCAGGCTCCCG
 GGACACCACGTGCATGGTGGGGCTCTGCATCAGGGTGGTCTGTCAGTAGGGCTGGCAC
 CAAAGCCCTGTCAGGCTCTGTATGGGCAAGGGCTGGCAGTGAGCTGTTGAGGCCATCAGCACT
 GAACTTGACATGGCTGTCTGGATCTGAGGATGGAACCTGTGATCATACACACTGTACGCCG
 CGGACAGTTGTAGCGGCAACTACGGCCTCTGGGTGCCACATCCCTGGACCTATTTCCACC
 TGGCATTGGGTCCGAAGGCCAGATTGTGGTACAGAGCTCAGCGTGGGAACGTCTGGGCC
 CAGGTACCCACTCCTGCACCTGTATTCAATGGGAAGTTGCGGGCTTCAC TGCC
 GGCAGAGCAGCCTACAGCCCTGACGGTACAGAGGACTTTGTGTTGCTGGCAGGCCAGT
 GCGCCCTGCAACATCCCAACTAAACACACTGCTCCGGCGCCTCCCTGCCCATGAAAG
 GTGGCCATCCGCAAGCGTGGCCGTGACCAAGGAGCGCAGGCCACGTGCTGGTGGGCCAGGGA
 TGGCAAGCTCATCGTGGTGGTGGCCGGCAGGCCCTGAGGTGCGCAGGCCAGTTCC
 GGAAGCTGTGGCGGTCTCGCGCGCATCTCCAGGTGTCCTCGGGAGAGACGGAATACAAC
 CCTACTGAGGCAGCGC**TGA**ACCTGGCCAGTCCGGCTGCTCGGGCCCCGGCAGGCCCTG
 GCCCGGGAGGGCCCCGGCCAGAAGTCGGGGAAACACCCGGGGTGGGAGGCCAGGGGTGA
 GCGGGGCCACCTGCCAGCTCAGGGATTGGCGGGGAGTGTACCCCTCAGGGATTGGCG
 GCGGAAGTCCCAGGCCCTGCGCCGGCTGAGGGGCCAGCAGCCACTGGCGT

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FIGURE 23

MSQFEMDTYAKSHDLMMSGFWNACYDMLMSSGQRRQWERAQSRRAFQELVLEPAQRRARLEGL
RYTAVLKQQATQHSMALLHWGALWRQLASPCGAVALRDTPIPRWKLSSAETYSRMRLKLVPN
HHFDPHLEASALRDNLGEVPLPTTEEASLPLAVTKEAKVSTPPELLQEDQLGEDELAELTP
MEAAELDEQREKLVLSAECQLVTVVAVVPGLEVTTQNVFYDGSTERVETEEGIGYDFRRP
LAQLREVHLRRFNLRSALELFFIDQANYFLNFPCKVGTPVSSPSQTPRPQPGPIPPHTQV
RNQVYSWLLRLRPPSQGYLSSRSRSPQEMLRASGLTQKWVQREISNFEYLMQLNTIAGRKYNDL
SQYPVFPWVLQDYVSPTLDLSNPAYFRDLSKPIGVVNPKHAQLVREKYESFEDPAGTIDKFH
YGTHYSNAAGVMHYLIRVEPFTSLHVQLQSGRFDCSDRQFHSAVAAWQARLESPADVKEIP
EFFYFPDFLENQNGFDLGCLQLTNEKVGDVVLPPWASSPEDFIQQHRQALESEYVSAHLHEW
IDLIFGYKQRGPAAEAEALNVFYCTYEGAVDLDHVTDERERKALEGIISNFGQTPCQLLKEP
HPTRLSAEEAAHRLARLDTNPSIFQHLDELKAFFAEVTVSASGLLGHWSLWYDRNISNYF
SFSKDPTMGSHKTQRLLSGPWPGSGVSGQALAVAPDGKLLFSGGHWDGSLRVTAALPRGKLL
SQLSCHLDVVTCLALDTCGIYLISGRDTTCMVWRLLHQGGLSVGLAPKPVQVLYGHGAAVS
CVAISTELDMAVSGSEDGTVIHTVRRGQFVAALRPLGATFPGPIFIHLALGSEGQIVVQSSA
WERPGAQVTYSLHLYSVNGKLRASLPLAEQPTALTVDFTVLLGTAQCALHILQLNTLLPAA
PPLPMKVAIRSVAVTKERSHVLVGLEDGKLIVVVAGQPSEVRSSQFARKLWRSSRRISQVSS
GETEYNPTEAR

N-glycosylation site.

amino acids 677-681

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 985-989

Tyrosine kinase phosphorylation site.

amino acids 56-65, 367-376, 543-551

N-myristoylation site.amino acids 61-67, 436-442, 604-610, 610-616, 664-670, 691-697,
706-712, 711-717, 769-775, 785-791, 802-808, 820-826, 834-840,
873-879, 912-918, 954-960

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FIGURE 24

CGGACGCGTGGCGGACGCGTGGGGCTGTGAGAAAGTCCAATAATACATCATGCAACCC
CACGGCCCACCTTGTGAACCTCTCGTGCCTAGGGCTGATGTGCGTCTTCAGGGCTACTCAT
CCAAAGGCCTAATCCAACGTTCTGTCTCAATCTGCAAATCTATGGGTCTGGGGCTCTTC
TGGACCCCTTAACGGTACTGGCCCTGGCCAATGCGTCCTCGCTGGAGCCTTGCCTCCTT
CTACTGGGCCTTCCACAAGCCCCAGGACATCCCTACCTCCCTTAATCTCTGCCTTCATCC
GCACACTCCGTTACCACACTGGGTACATTGGCATTGGAGCCCTCATCCTGACCCCTGTGCAG
ATAGCCCAGGTACATTGGAGTATATTGACCACAAGCTCAGAGGAGTGCAGAACCTGTAGC
CCGCTGCATCATGTGCTGTTCAAGTGCTGCCTCTGGTGTCTGGAAAAATTATCAAGTTCC
TAAACCGCAATGCATACATCATGATGCCATCTACGGGAAGAATTCTGTGTCTAGCCAAA
AATGCGTTCATGCTACTCATGCGAACATTGTCAGGGTGGTGTCTGGACAAAGTCACAGA
CCTGCTGCTGTTCTGGGAAGCTGCTGGTGGTGGAGGCGTGGGGGCTGTCCCTCTT
TTTCTCCGGTCGCATCCCAGGGCTGGTAAAGACTTTAAGAGCCCCACCTCAACTATTAC
TGGCTGCCCATCATGACCTCCATCCTGGGGCCTATGTCATGCCAGCGGCTTCTCAGCGT
TTCGGCATGTGTGGACACGCTCTCCTCTGCTTGGAAAGACCTGGAGCGGAACAAACG
GCTCCCTGGACCGGCCCTACTACATGTCCAAGAGCCTCTAAAGATTCTGGCAAGAAGAAC
GAGGCGCCCCCGACAACAAGAAGAGGAAGTGACAGCTCCGGCCCTGATCCAGGACTGC
ACCCCAACCCCCACCGTCCAGCCATCCAACCTCACTTCGCTTACAGGTCTCCATTGTGGT
AAAAAAAGGTTTAGGCCAGGCGCCGTGGCTACGCCTGTAATCCAACACTTGAGAGGCTG
AGGCGGGCGGATCACCTGAGTCAGGAGTCAGGAGACCAGCCTGGCAACATGGTAAACCTCC
GTCTCTATTAAAAATACAAAAATTAGCCGAGAGTGGTGGCATGCACCTGTCTCCAGCTAC
TCGGGAGGCTGAGGCAGGAGAATCGCTGAACCCGGGAGGCAGAGGTTGCAGTGAGCCGAGA
TCGCGCCACTGCACTCCAACCTGGGTGACAGACTCTGTCTCCAAAACAAAACAAACAA
AAAGATTTATTAAAGATATTGTAACTC

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FIGURE 25

RTRGRTRGGCEKVPINTSCNPTAHLVNSSCPGLMCVFQGYSSKGLIQRSVFNLQIYGVLGLFWTLNWVLALGQCVLAGAFASFYWAFHKPQDIPTFPLISAFIRTLRYHTGSLAFGALILTLVQIARVILEYIDHKLRGVQNPVARCIMCCFKCCLWCLEKFIKFLNRNAYIMIAIYGKNFCVSAKNAFMLLMRNIVRVVVLDKVTDLLLFFGKLLVVGGVGVLSSFFSGRIPGLGKDFKSPHLNYYWLPIMTSILGAYVIASGFFSVFGMCVDTLFLCFLEDLERNNNGSLRPYYMSKSLLKILGKKN
EAPPDNKKRKK

FIGURE 26

GAGTCTTGACCGCCGCCGGCTCTGGTACCTCAGCGCGAGCGCCAGGCAGCCGGTCCGGCG
GGCTATGTTCGTGTCCGATTCCGCAAAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGTCC
TTCTCTCGTGGCCTCGGACGTGGATGCTCTGTGTGCGTCAAGATCCTCAGGCCTGTT
CAGTGTGACCACGTGCAATATAACGCTGGTCCAGTTCTGGTGGCAAGAACTTGAAACTGC
ATTCTTGAGCATAAAGAACAGTTTCAATTCTCATAAACTGTGGAGCTAATGTAG
ACCTATTGGATATTCTCAACCTGATGAAGACACTATATTCTTGACTCCATAGG
CCAGTCATGTCGTCAATGTATACAACGATAACCGATCAAATTACTCATTAAACAAGATGA
TGACCTGAAGTTCCCGCTATGAAGACATCTCAGGGATGAAGAGGAGGATGAAGAGCATT
CAGGAAATGACAGTGATGGTCAGAGCCTCTGAGAAGCGCACACGGTTAGAAGAGGAGATA
GTGGAGCAAACCATGCGGAGGAGGCAGCGCGAGAGTGGGAGGCCGGAGAAGAGACATCCT
CTTGACTACGAGCAGTATGAATATCATGGACATCGTCAGCCATGGTGTGACTGG
CTTGGATGCTGTCCAAGGACCTGAATGACATGCTGTGGTGGCCATCGTGGACTAACAGAC
CAGTGGGTGCAAGACAAGATCACTCAAATGAAATACGTGACTGATGTTGGTGTCTGCAGCG
CCACGTTCCCGCCACAACCACCGAACGAGGATGAGGAGAACACACTCTCCGTGGACTGCA
CACGGATCTCCTTGAGTATGACCTCCGCTGGTGTCTACCAGCACTGGTCCCTCCATGAC
AGCCTGTGCAACACCAGCTATAACCGCAGCCAGGTTCAAGCTGTGGTGTGCATGGACAGAA
GCGGCTCCAGGAGTCCCTGCAGACATGGCTTCCCTGAAGCAGGTGAAGCAGAAGTTCC
AGGCCATGGACATCTCCTGAAGGAGAATTGCGGGAAATGATTGAAGAGTCTGCAAATAAA
TTTGGGATGAAGGACATGCGCGTGCAGACTTCAGCATTCAATTGGTCAAGCACAAGTT
TCTGGCCAGCGACGTGGTCTTGCCACCATGTCTTGATGGAGAGCCCGAGAAGGATGGCT
CAGGGACAGATCACTCATCCAGGCTCTGGACAGCCTCTCCAGGAGTAACCTGGACAAGCTG
TACCATGGCCTGGAACTGCCAAGAACGAGCTGCGAGCCACCCAGCAGACCATTGCCAGCTG
CTTGACCAACCTCGTCATCTCCAGGGCTTCTGTACTGCTCTCATGGAGGGCAC
TCCAGATGTCATGCTGTTCTAGGCCGGCATCCCTAACGCTGCTCAGCAAACACCTGCTCA
AGTCCTTGTGTTGACAAAGAACCGCGCTGCAAACACTGCTGCCCTGGTATGGCTGCC
CCCCTGAGCATGGAGCATGGCACAGTGACCGTGGTGGCATCCCCCAGAGACCGACAGCTC
GGACAGGAAGAACCTTTGGAGGGCGTTGAGAAGGCAGCGGAAGCACCAGCTCCCGGA
TGCTGCACAACCATTGACCTCTCAGTAATTGAGCTGAAAGCTGAGGATCGGAGCAAGTT
CTGGACGCACCTATTCCCTCGTCCTAGGAATTGATTCTCCAGAATGACCTCTTATT
TATGTAACTGGCTTCATTAGATTGTAAGTTATGGACATGATTGAGATGTAGAAGCCATT
TTTATTAAATAAAATGCTTATTAGGAAA

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FIGURE 27

MFVSDFRKEFYEVVQSRVLLFVASDVLCAKILQALFQCDHVQYTLVPVSGWQELETAFL
LEHKEQFHYFILINCGANVDLLDILQPDEDTIFFVCDSHRPVNVNLYNDTQIKLLIKQDDD
LEVPAYEDIFRDEEEDEEHSGNDSGSEPKTRLEEEIVEQTMRRQRREWEARRDILF
DYEQYEYHGTSAMVMFELAWMLS KDLNDMLWWAIVGLTDQWVQDKITQMKYVTDVGVLQRH
VSRHNHRNEDEENTLSVDCTRISFEYDLRLVLYQHWSLHDSDLNTSYTAARFKLWSVHGQKR
LQEFLADMGLPLKQVKQKFQAMDISLKENLREMIEESANKFGMKDMRVQTFSIHFGFKHKFL
ASDVFATMSL MESPEKDGS GTDHFIQALDSLSRSNLDKLYHGLELAKKQLRATQQTIASCL
CTNLVISQGPFLYCSLMEGTPDVMLFSRPASLSSLLSKHLLKSFVCSTKNRRCKLLPLVMAAP
LSMEHGTVTVVGIPPETDSSDRKNFFGRAFEKAAESTSSRMLHNHF DLSVIELKAEDRSKFL
DALISLLS

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FIGURE 28

GTACCTCAGCGCGAGCGCCAGCGTCCGGCCGCCGTGGCTATGNTCGTGTCCGATTCCGCA
AAGAGTTCTACGAGGTGGTCCAGAGCCAGAGGGCCTCTCTCGTGGCCTCGGANGTGGAT
GCTCTGTGTGCGTGCAAGATCCTTCAGGCCTTGTCCAGTGTGACCANGTGAATATANGCT
GGTTCCAGTTCTGGGTGGCAAGAACTTGAAACTGCATTCTTGAGCATAAAGAACAGTTTC
ATTATTTATTCTCATAAACTGTGGAGCTAATGTAGACCTATTGGATATTCTTCAACCTGAT
GAAGACACTATATTCTTGTGTGACACCCATAGGCCAGTCAATGTTGTCAATGTATACAA
CGATACCC

FIGURE 29

CAGGAACCCTCTTTGGTCTGGATTGGGACCCCTTCCAGTACCATTTCTAGTGAAC
CACGAAGGGACGATACCAGAAAACACCCCTCAACCCAAAGGAATAGACTACAGCCCCAATTG
GCTGACTTTGGCTATAGAAAAAAGAAAGAACGAAAAGAGACAGTTTTGGAAAGCTAA
GTCTTCCCTTATCGAGTCAGAAACCCCCCTCTTGAGCTATTACAGCTTTAACATT
GAGTAAAGTACGCTCCGGTACCCATGGTACAGGCCCTGGTCCCGTCTGGCAGCGCTC
CTGCTCTTCTCCTGATGTGAGATCCGTATGGTGGAGCTCACCTTGACAGAGCTGTGGC
CAGCGGCTGCCAACGGTCTGTGACTCTGAGGACCCCTGGATCCTGCCATGTATCCTCAG
CCTCTCCTCCGGCCGCCACGCCCTGCCTGAGATCAGACCCATCATTAATATCACCATC
CTGAAGGGTACAAAGGGGACCCAGGCCAATGGGCTGCCAGGGTACATGGGAGGGAGGG
TCCCCAAGGGGAGCCTGGGCTCAGGGCAGAAGGGTACAAGGGGAGATGGGAGGCCCG
GCGCCCCGTGCCAACAGCCTTCAGCCTCTCAGTGGGCCAGAACAGGCCCTGCACAGC
GGCGAGGACTCCAGACGCTCTCGAAAGGGTCTTGATGGGTGCTTTGA
CATGGCAGCCAGTTCAGTGTCTCCCTGCGTGGCATCTACTTCTCAGCCTCAATGTGC
ACAGCTGAAATTACAAGGAGACGTACGTGCACATTATGCATAACCAGAAAGAGGCTGTAC
CTGTACGCGCAGCCAGCGAGCGCAGCATCATGCAGAGCCAGAGTGTGATGCTGGACCTGGC
CTACGGGACCGCGTCTGGTGCCTCTCAAGGCCAGCGAGAACGCCATCACAGCA
ACGACTTCGACACCTACATCACCTCAGGCCACCTCATCAAGGCCAGGACGACT**TA**GGG
CCTCTGGGCCACCCCTCCGGCTGGAGAGCTCAGGTGCTGGTCCCGTCCCTGCAGGGCTCAG
TTGCACTGCTGTGAAGCAGGAAGGGCAGGGAGGTCCCGGGACCTGGCATTCTGGGAGA
CCCTGCTTCTATCTGGCTGCCATCATCCCTCCAGCCTATTCTGCTCTCTTCTCT
TGGACCTATTAAAGAAGCTTGTAAACCTAAATATCTAGAAACTTCCCAGCCTCGTAGCCC
AGCACTCTCAAACCTGGAAATGCATGCCAATCACCCGGGTTCGTGTAAATGCAGATTCT
GACTCAGCAGGTCTGAGTGGTCCAGGATTCTGTGTTCTCATATGTTCTGGGTGATGCTG
ATGGGGTCAGTCTATGAACCACACTGGAGCAACCAGGTTCTAGGACTTTCTCAATATTCTAG
TACTTCTGAACATTGGAATCCCTCCACATTCTAGAATTCTCCAACATTTTTTCT
TGAGACAGAGCTTGCTCTGGTGCCTGGCAGGCTAGAGTGCAGTGGTCAATCTCAGTTACTGC
AACCTCTGCCTCCGGGTTCAAGCAGATTCTCTGCCTCAGCCTCCAGTGGCTGGGATTAC
AGGCCTGCTACCATGCCCTGGTAATTGGTATTCTAGAGATGGGTTACCCATA
TTGGCCAGGTGGTCTTGAACCTCTGACTCAGGTGACCCACCCGCCTGGCCTCTCAAAT
GCTGGGATTACAGGTGTGAGCCACCGTGCCTGGCCAATTCAAACATTCTAAATTCTCAT
CCCTCCAGGGCTCCCGTGCTATGTTCTTACCCCTTCCCTCTTGTCTCAGGCC
TGCACCACTGCAGCCACCGTTCTTATTCTATTCAAAACACTGAGCACTCACTGTGCT
GGTCCCAGGGAGGGTGGAGGGGTCAGACACAGGCCCTGCCCTCAGTGAUTGGCCA
GTCAGGCCAGGGAGAGATGTGACATAGGTTAAAGCAGACCCAGAGCTCATGGGG
GCCGTGTTCTGGGTGTTCAAGGTGCTGCTGGTCCATTACCCACTGCTCCCCAAGGCTGG
TGGGACGGGGCTCCCGGTGGCAGGGCAGGTATCTCTTCCCTCATCCACCTGCCAG
TGCTCATGTTACAGCAAACCCAGGGGCTTGGCCAGGTCAAGGGTTCTGTGAGGAGAGG
ACCCAGGAGTGTGGGGGATTGGGGGTGAAGTGGCCCCGAAGAATGGAACCCACACCA
TAGCTCTCCCCACAGCTGATACGGCATCTGCAGAGAACCTGCCCTCCACTGGATCCC
CTTCCTGCCTCCCTCCAGGGCTGTGCCAGGGCCTGCTCAGTCCCTCCACCAAAGTCATCT
GAACCTCCGTTCCCCAGGGCCTCCAGCTGCCCTCAGACACTGATGTCTGCTCCAGGTGCT
CTCTGCCCTCATGCCCTCTCACCGGCCAGTGCCTGACTCTCCAGGCTTATCAAGGTG
CTAAGGGGGGGTGGCAGCTCTCGTCTCAGAGGCCCTCCGGCTGGTCTGCCCTTAC
AAACACCTGCAGGAGAAGGGCCACGGAAGCCCCAGGCTTAAAGGCCCTCAGCAGGTCTGGGG
AGCTAGAGCAAAGGAGGGACCTCAGGCCCTCCAGGTGGCCTGCCCTCTCCAGGGTGGGGTGGCCTGGT
GTTCCCTAGCCTCCAAACCCAGGTGGCCTGCCCTCTCCAGGGGAGGGAGGCCCTCCGC
CCATTGGTGCCTCATGCAGACTCTGGGCTGAGGTGCCCGGGGGTGAATCTGGTGCCTCAC
AGCCGAGGGAGCCGTGGCTCCATGGCAGATGACGGAAACAGGGTCTGACCAAGTGCAGGA
AGACCTGTGTATAAACACCCTGCCTGATCCTGCCCTGCTGACCCGCCAGGCCCTGCC
GTCCAGCATGATTAAGAATGCTGTCTCTTGGAAAAA

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FIGURE 30

MVTAALGPVWAALLLFLLMCEIRMVELTFDRAVASGCQRCCDSEDPLDPAHVSSASSSGRPH
ALPEIRPYINITILKGDKGDPGPMGLPGYMGREGPQGEPPGQGSKGDKGEMGSPGAPCQKRF
FAFSVGRKTALHSGEDFQTLLFERVFVNLDGCFDMATGQFAAPLRGIYFFSLNVHSWNYKET
YVHIMHNQKEAVILYAQPSERSIMQSQSVMLDLAYGDRVWVRLFKRQRENAIYSNDFDTYIT
FSGHLIKAEDD

Important features:

Signal peptide:

amino acids 1-20

N-glycosylation site.

amino acids 72-75

C1q domain proteins.

amino acids 144-178, 78-111 and 84-117

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FIGURE 31

ACTCGAACGCAGTTGCTCGGGACCCAGGACCCCTCGGGCCCGACCCGCCAGGAAAGACTG
AGGCCGCGGCCCTGCCCGCCGGCTCCCTGCGCCGCCGCCCTCCGGGACAGAAGATGTG
CTCCAGGGTCCCTCTGCTGCTGCCGCTGCTCCCTGCTACTGGCCCTGGGGCCTGGGTGCAGG
GCTGCCCATCCGGCTGCCAGTGCAGCCACAGACAGTCTCTGCACTGCCGCCAGGG
ACCACGGTCCCCGAGACGTGCCACCCGACACGGTGGGCTGTACGTCTTGAGAACGGCAT
CACCATGCTCGACGCAGGCAGCTTGCGGCCCTGCCGGGCTGCAGCTCTGGACCTGTCAC
AGAACCCAGATGCCAGCCTGCCAGCGGGTCTCCAGCCACTGCCAACCTCAGAACCTG
GACCTGACGCCAACAGGCTGCATGAAATACCAATGAGACCTTCCGTGGCCTGCCGCCT
CGAGGCCCTACCTGGGCAAGAACCGCATCCGCCACATCCAGCCTGGTGCCTTGACACGC
TCGACCGCCTCTGGAGCTCAAGCTGCAGGACAACGAGCTGCCGACTGCCCGCTGCC
CTGCCCGCCCTGCTGCTGCCACTCAGCCACAACAGCCTCTGGCCCTGGAGGCCGCAT
CCTGGACACTGCCAACGTGGAGGCCTGCCGCTGGCTGGCTGGGCTGCAGCAGCTGGACG
AGGGGCTCTCAGCCGCTTGCGCAACCTCACGACCTGGATGTGTCGACAACCAGCTGGAG
CGAGTGCCACCTGTGATCCGAGGCCTCCGGGCTGACGCCCTGCCGCTGGCCGGCAACAC
CCGCATTGCCAGCTGCCGGGAGGACCTGCCGCCCTGGCTGCCCTGCAGGAGCTGGATG
TGAGCAACCTAACGCTGCAGGCCCTGCCCTGGCGACCTCTCGGCCCTTCCCCGCCCTGCC
CTGCTGGCAGCTGCCGCAACCCCTCAACTGCGTGTGCCCTGAGCTGGTTGGCCCGCTG
GGTGCAGAGGCCACGTCACACTGCCAGCCCTGAGGAGACGCCGCTGCCACTTCCCGCCA
AGAACGCTGCCGGCTGCTCCTGGAGCTGACTACGCCGACTTTGGCTGCCAGGCCACC
ACCACAGCCACAGTGCCACACGCCAGAGGCCGAGCCCTGGTGCAGGAGGCCACAGCCTTG
CTTGGCTCCTACCTGGCTTAGCCCCACAGGCCGGCCACTGAGGCCAGGACTGCCACCGT
CTGCCCTGCCACTGTAGGGCCTGTCCCCCAGGCCAGGACTGCCACCTGCCCT
AATGGGGCACATGCCACCTGGGACACGGCACCACCTGGCGTGTGCTGGCCGAAGGCTT
CACGGGCTGTACTGTGAGAGCCAGATGGGGCAGGGGACACGCCCTACACCAGTC
CGCCGAGGCCACCACGGTCCCTGACCTGGCATCGAGCCGGTGAAGGCCACCTCCCTGCC
GTGGGGCTGCCAGCGCTACCTCCAGGGGAGCTCGTGCAGCTCAGGAGCCTCGTCTCAC
TCGCAACCTATCGGCCCTGATAAGCGGCTGGTGAACGCTGCGACTGCCCTGCCCTCG
AGTACACGGTCACCCAGCTGCCGCCAACGCCACTTACTCCGTCTGTGATGCCCTGGGG
CCCGGGCGGGTGCCGGAGGGCAGGAGGCCCTGCCGGGAGGCCACACCCCCAGCCG
CTCCAACCACGCCCAAGTCACCCAGGCCCGAGGGCAACCTGCCCTCATTGCC
CCCTGGCCCGGTGCTCTGGCCCGCTGGCTGCCGGTGGGGCAGCCTACTGTGCGGCC
GGCGGGGCCATGGCAGCAGCGGCTCAGGACAAAGGGCAGGTGGGGCAGGGCTGGGCC
GGAACCTGGAGGGAGTGAAGGTCCCTGGAGGCCAGGCCAGGCAACAGAGGGCG
AGGCCCTGCCAGCGGGTCTGAGTGTGAGGTGCCACTCATGGCCTCCAGGCCCTGGC
CAGTCACCCCTCCACGCAAAGCCCTACATCTAAGCCAGAGAGAGACAGGGCAGCTGGGCC
GGCTCTCAGCCAGTGAAGATGGCCAGGCCCTCTGCTGCCACACCACGTAAGTCTCAGTCC
CAACCTCGGGGATGTGTCAGACAGGCCCTGCTGCCACACCACGTAAGTCTCAGTCC
CCTCGGTCTCCTCATCTGTGAGATGCTGGCCAGCTGACGAGGCCCTAACGTCCCCAGAAC
CGAGTGCCTATGAGGACAGTGTCCGCCCTGCCCTCCGCAACGTGCAGTCCCTGGGCACGGCG
GGCCCTGCCATGTGCTGGTAACGCACTGCCCTGGTCTGCTGGCTCTCCACTCCAGGCC
CCCTGGGGGCCAGTGAAGGAAGCTCCCGAAAGAGACAGAGGGAGAGCGGGTAGGCC
TGACTCTAGTCTTGGCCCCAGGAAGCAAGGAACAAAGAAACTGGAAAGGAAGATGCTTA
GGAACATGTTTGTCTTTAAAAATATATATTTAAGAGATCCTTCCATTATTCTG
GGAAGATGTTTCAAACCTCAGAGACAAGGACTTGGTTTGTAAAGACAAACGATGATATG
AAGGCCCTTGTAAAGAAAAAATAAAAGATGAAGTGTGAAA

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FIGURE 32

MCSRVPLLLPLLLLALGPGVQGCPSCQCSQPQTVFCTARQTTVPRDVPPDTVGLYVFEN
GITMLDAGSFAGLPGLQLLDSQNQIASLPSGVFQPLANLSNLDLTANRLHEITNETFRGLR
RLERLYLGKNRIRHIQPGAFDTLDRLELKLQDNELRALPPLRLPRLLLLDSHNSLLALEP
GILDTANVEALRLAGLGLQQLDEGLFSRLRNLHLDVSDNQLERVPPVIRGLRGLTRLRLAG
NTRIAQLRPEDLAGLAALQELDVSNLSQLPGDLSGLFPRLRLLAAARNPFNCVCPLSWFG
PWVRESHVTLASPEETRCHFPPKNAGRLLLELDYADFGCPATTTATVPTTRPVVREPTALS
SSLAPTWLSPTAPATEAPSPPSTAPPTVGVPVPQDCCPPSTCLNGGTCHLGTRHHLACLCPE
GFTGLYCESQMGGTTRPSPTPVTPRPPRSLTGLIEPVSPSLRVGLQRYLQGSSVQLRSLRL
TYRNLSGPDKRLVTLRLPASLAEYTVTQLRPNATYSVCVMPLGPGRVPEGEEACGEAHTPPA
VHSNHAPVTQAREGNLPLLIAPALAAVLLAALAAVGAAYCVRRGRAMAAAAQDKGQVGPAG
PLELEGVKVPLEPGPKATEGGGEALPSGSECEVPLMGFPGLQSPFHAKPYI

FIGURE 33

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FIGURE 34

MRLIRNIYIFCSIVMTAEGDAPELPEEREELMTNCNSMSLRKVPADLTATTLDLSYNLLFQ
LQSSDFHSVSKLRVLILCHNRIQQQLDLKTFEFNKELRYLDLSNNRLKSVTWYLLAGLRYLDL
SFNDFDTMPICEEAGNMSHLEILGLSGAKIQKSDFQKIAHLHNTVFLGFRTLPHYEEGSLP
ILNTTKLHIVLPMDTNFWVLLRDGIKTSKILEMTNIDGKSQFVSYEMQRNLSLENAKTSVLL
LNKVDLLWDDLFLILQFWHTSVEHFQIRNVTGGKAYLDHNSFDYSNTVMRTIKLEHVHFR
VFYIQQDKIYLLLTKMDIENLTISNAQMPHMLFPNYPTKFQYLNFANNILTDELFKRTIQLP
HLKTLILNGNKLETLSVSCFANNTPLEHLDLSQNLLQHKNDENCSWPETVVNMNLSYNKLS
DSVFRCLPKSIQILDNNNQIQTVPKETIHLMALRELNIAFNFLTLPGCSHFSRLSVLNIE
MNFILSPSLDFVQSCQEVKTLNAGRNPFRCTCELKNFIQLETYSEVMMVGWSDSYTCEYPLN
LRGTRLKDVLHHELSCNTALLIVTIVVIMVLGLAVAFCCCLHFDLPWYLRMLGQCTQTWHRV
RKTTQEQLKRNVRFHAFISYSEHDSLWVKNELIPNLEKEDGSILICLYESYFDPGKSISENI
VSFIEKSYKSIFVLSNFVQNEWCHYEFYFAHHNLFHENSDHIIILILLEPIPFYCIPTRYHK
LKALLEKKAYLEWPKDRRKCGFWANLRAAINVNVLATREMYELQFTTELNEESRGSTISLM
RTDCL

FIGURE 35

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FIGURE 36

MSRPGTATPALALVLLAVTLAGVGAQGAALEDPDYYGQEIWREPYYARPEPELETFSPPPLP
AGPGEEWERRPQEPRPPKRATKPKKAPKREKSAPEPPPGKHSNKKVMRTKSSEKAANDDHS
VRVAREDVRESCPPLGLETLKITDFQLHASTVKRYGLGAHRGRLNIQAGINENDFYDGAWCA
GRNDLQQWIEVDARRLTRFTGVITQGRNSLWLSDWVTSYKVMVSNDSHWTWTVKNGSGDMIF
EGNSEKEIPVLNELPVPMVARYIRINPQSWFDNGSICMRMEILGCPLPDPNNYYHRRNEMTT
TDDDFKHHNYKEMRQLMKVVNEMCPNITRIYNIGKSHQGLKLYAVEISDHGEHEVGEPEF
HYIAGAHGNEVLGRELLLLVQFVCQEYLARNARIHLVEETRIHVLPSSLNPDGYEKAYEGG
SELGGWSLGRWTHDGIDINNNFPDLNTLLWEAEDRQNVPRKVPNHYIAIPEWFLSENATVAA
ETRAVIAWMEKIPFVLGGNLQGGELVVAYPYDLVRSPWKTQEHTPTPDDHVFRWLAGSYAST
HRLMTDARRVCHTEDFQKEEGTVNGASWHTVAGSLNDFSYLHTNCFELSIYVGCDKYPHES
QLPEEWENNRESLIVFMEQVHRGIKGLVRDSHGKGIPNAIISVEGINHDIRTANDGDYWRLL
NPGEYVVTAKAEGFTASTKNCMVGYDMGATRCDFTLSKTNMARIREIMEKFGKQPVSLPARR
LKLGRGRKRRQRG

FIGURE 37

CTAAGAGGACAAGATGAGGCCGGCTCTCATTCTCTAGCCCTCTGTTCTCCAGGCCAGCTGCAGGGG
ATTGGGGGATGTGGACCTCAATTCCAGCCGGCTCAGCTCTTCCAGGTGTTGACTCAGCTCCAGC
TTAGCTCCAGCTCCAGGTGGCTCAGCTCCAGCCAGCTAGGAGGGCTGTGTTCCAGTTGTT
TTCCAATTCCACCGCTCCGTGGATGACCGTGGACCTGCCAGTGCTGTGTTCCCTGCCAGACACCACCTTC
CCGTGGACAGAGTGGAACGCTTGAATTACAGCTCATGTTCTTCTAGAAGTTGAGAAAGAAACTTCTAAA
GTGAGGGAAATATGTCCAATTAAATTAGTGTGATGAAAAGAAACTGTTAAACCTAACTGTCCGAATTGACATCAT
GGAGAAGGATACCATTCTACACTGAACACTGGACTTCAGGCTGATCAAGGATAGAAGTGAAGGAGATGGAAAAC
TGGTCATACAGCTGAAGGAGAGTTGGTGGAAAGCTAGAAATTGTTGACCAGCTGGAGGTGGAGATAAGAAAT
ATGACTCTCTGGTAGAGAACGACTTGAGACACTAGACAAAACAATGTCCTGCCATTGCCAGAAATCGTGGC
TCTGAAGACCAAGCTGAAGAGTGTGAGGCCCTCTAAAGATCAAACACCCTGTCGCCCCCTCCACTC
CAGGGAGCTGGGTGATGGTGGTGGTAACATCAGCAAACCGCTGTTGAGCTCAGCTCAACTGGAGAGGGTT
TCTTATCTATATGGTCTGGGGTAGGGATTACTCTCCCCAGCATCAAACAAAGGACTGTATTGGGTGGCGCC
ATTGAATACAGATGGGAGACTGTGGAGTATTAGACTGTACAACACACTGGATGATTGCTATTGTATATAA
ATGCTCGAGAGTTGGGATCACCTATGCCAAGGTTAGGTGATGGTACAAGCTGGTATGACAACAAACATGTACGTCAC
ATGTAACACCGGAATATTGCCAGGTTAACCTGACCAACACGATTGCTGTGACTCAAACCTCTCCCTAA
TGCTGCCATAATAACCGTTTCATATGCTAATGTTGCTGGCAAGGATATTGACTTTGCTGTGATGAGAATG
GATTGTGGGTTATTATTCAACTGAAGCCAGCAGTGGTAACATGGTGTAGTAAACTCAATGACACCACACT
CAGGTGCTAAACACTTGGTATACCAAGCAGTATAAACCATCTGCTCTAACGCCCTCATGGTATGGGGTTCT
GTATGCCACCGTACTATGAACACCAGAACAGAGATTTTACTATTATGACACAAACACAGGGAAAGAGG
GCAAACACTAGACATTGTAATGCATAAGATGCAGGAAAAGTCAGAGCATTAACATAACCTTTGACCAGAAA
CTTATGTCTATAACGATGGTACCTCTGAATTATGATCTTCTGTCTGCAGAAGCCCCAGAAGCTGTTA
GGAGTTAGGGTAAAGAGAAAATGTTGTTGAAAAAAATAGTCTCTCCACTTACTAGATATCTGAGGGGTGT
CTAAAAGTGTGTTCATTTGCAGCAATGTTAGGTGCACTAGTCTACCACACTAGAGATCTAGGACATTGCT
TGATTGGTGAGTTCTCTGGGATCATCTGCCCTTCAGGCCATTGCAATAAGCTGTCTAGGGTGGGA
TTGTCAGAGGTCTAGGGGACTGTGGGCCTAGTGAGCCTACTGTGAGGGGCTTCACTAGAAGCCTAAATTA
GGAATTAAGGAACTTAAACACTGAGTGGCTAGGGATTCTTGTCAGGAAATATTGCCCAATGACTAGTC
CTCATCCATGTAGCACCCTAAATTCTCCATGCCGAAAGAACCTGGGGACTTAGTTAGGTAGATTAAATATCT
GGAGCTCTCGAGGGACCAAATCTCAAACCTTTTCTCCACTAGCACCCTGGAATGATGCTTGTATGTGG
CAGATAAGTAATTGGCATGCTTATATATTCTACATGTAAAGTGTGAGTTATGGAGAGAGGCCCTTTT
ATGCATTAATTGTACATGGCAAATAATCCCAGAAGGATCTGTAGATGAGGCACCTGCTTTCTTCTC
ATTGTCCACCTACTAAAGTCAGTAGAATCTTACCTCTACACTTCCAAAGGCAGCTCAGAAGATTAG
AACCAGACTACTAACCAATTCCACCCCCCACCACCCCTCTACTGCCTACTTTAAAAAAATAATAGTTT
CTATGGAACTGATCTAAGATTAGAAAATTAAATTCTTAAATTCTTACATTATGGACTTTATTTACATGACTCTA
AGACTATAAGAAAATCTGATGGCAGTGACAAAGTGTAGCATTATTGTTATCTAATAAGACCTGGAGCATA
TGTGCAACTTATGAGTGTATCAGTTGTCATGTAATTGCTTGCCTTGTTAAGCCTGGAACTTGTAAAGAAAAT
GAAAATTAAATTCTAGGAGCAGCTATAGAAAAGCTATTGAGAGTATCTAGTTAAATCAGTGCAGTAGT
TGGAACCTTGTGCTGGTGTATGTGATGTGCTTCTGTGCTTTGAATGACTTTATCATCTAGTCTTGTCTATT
TCCCTTGATGTCAAGTCAGTCTATAGGATTGGCAGTTAAATGCTTACTCCCCCTTTAAATAAATGAT
TAAATGTGTTGAAAAA

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FIGURE 38

MRPGLSFLLALLFFLGQAAGDLGDVGPPIPSPGFSSFPGVDSFFFSSSRSGSSSRSLGS
GGSVSQLFSNFTGSVDRGTCQCSVSLPDTFPVDRVERLEFTAHVLSQKFEKELSKVREYV
QLISVYEKLLNLTVRIDIMEKDTISYTTELDFELIKVEVKEMEKLVIQLKESFGGSSEIVDQ
LEVEIRNMTLLVEKLETLDKNNVLAIRREIVALKTKLKECEASKDQNTPVVHPPPTPGSCGH
GGVVNISKPSVQLNWRGFSYLYGAWGRDYSPOHNPGLYVAPLNTDGRLEYYRLYNTLD
DLILYINARELRITYGQGSGTAVYNNNMYVNMYNTGNIARVNLTNTIAVTQTLPNAAYNNR
FSYANVAWQDIDFAVDENGLWVIYSTEASTGNMVISLNDTTLQVLNTWYTKQYKPSASNAF
MVCGVLYATRTMNTRTEEIFYYYDTNTGKEGKLDIVMHKMQEKVQSINYNPFDQKLYVYNDG
YLLNYDLSVLQKPQ

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FIGURE 39

GCTCTGAAGACCAAGCTGAAAGAGTGTGAGGCCTCTAAAGATCAAACACCCCTGTCGTCCAC
CCTCCTCCCCTCCAGGGAGCTGTGGTCAATGGTGGTGTGGTGAACATCAGCAAACCGTCTGT
GGTCAGCTCAACTGGAGAGGGTTTCTTATCTATGGTGCTTGGGTAGGGATTACTCTC
CCCAGCATCCAAACAAAGGNATGTATTGGGNGGCCATTGAATAACAGATGGGAGACTGTTG
GAGTATTATAGACTGTACAACCCACTGGATGATTGCTATTGTATATAATGCTCGAGAGTT
GCGGATCACCTATGCCAAGGTAGTGGTACAGCAGTTACAACAACATGTACGTCAACA
TGTACAACACCGGGNATATTGCCAGAGTTAACCTGACC

FIGURE 40

TCTCGCAGATAGTAAATAATCTCGGAAAGGCAGAGAAAGAAGCTGTCTCCATCTTGTCTGTAT
 CCGCTGCTCTTGTGACGTTGGAGATGGGAGCGCTCTGGGCCTGTGCTCCATGGCGAGCT
 GGATACCATGTTGTGGAAGTGCCTGGCTTGTCTATGCCATGCTGCTTAGTGGAAAC
 AACTCCACTGTAACTAGATTGATCTATGCACTTTCTTGTGCTGGAGATGTGAGCTTG
 TGTAAATGTTGATACCAAGGAATGGAAGAACAACTGAATAAGATTCTGGATTTGTGAGAATG
 AGAAAAGGTGTTGTCCTGTAAACATTTGGTGGCTATAAAGCTGTATATCGTTGTGCTTT
 GGTTGGCTATGTTCTATCTTCTCTTACTAATGATCAAAGTGAAGAGTAGCAGTGA
 TCCTAGAGCTGCAGTCACAATGGATTTGGTCTTAAATTGCTGCAGCAATGCAATT
 TTATTGGGGCATTCTTCATTCCAGAAGGAACCTTTACAACAGTGTGTTGGTTATGTAGGCATG
 GCAGGTGCCCTTGTTCATCCATACAACTAGTCTTACTATTGATTTGCACATTGATG
 GAATGAATCGTGGTTGAAAAAAATGGAAGAGGAACCTGAGATGTTGGTATGCAGCCTTGT
 TATCAGCTACAGCTGAAATTATCTGCTGTTAGTTGCTATCGTCCTGTTCTGCTAC
 TACACTCATCCAGCCAGTTGTCAGAAAACAAGGCAGTCATCAGTGTCAACATGCTCCTCTG
 CGTTGGTGCCTCTGTAATGTCATACTGCCAAAATCCAAGAACATACAACCAAGATCTGGTT
 TGTACAGTCTTCAGTAATTACAGTCAACAAATGTATTGACATGGTCAGCTATGACCAAT
 GAACCAAGAACAAATTGCAACCAAGTCACTAACGATAATTGGCTACAATACAACAGCAC
 TGTCCTAAAGGAAGGCAGTCAGTCCAGTGGCATGCTCAAGGAATTATAGGACTAATT
 TCTTTTGTTGTGTTGATTTTATTCCAGCATCGTACTTCAAACAAATAGTCAGGTTAATAAA
 CTGACTCTAACAAAGTGTGAATTCTACATTAATAGAAGATGGTGGAGCTAGAAGTGTGATGGATC
 ACTGGAGGATGGGACGATGTTCACCGAGCTGTAGATAATGAAAGGGATGGTGTACTTACA
 GTTATTCTCTTCACTCATGCTTCTGGCTTCACTTATATCATGATGACCCCTTACC
 AACTGGTCCAGGTATGAAACCTCTCGTGAGATGAAAAGTCAGTGGACAGCTGTCGGGTGAA
 AATCTCTTCAGTTGGATTGGCATCGTGCTATGTTGGACACTCGTGGCACCCTGTTC
 TTACAAATCGTGAATTGACTTGAGACTTCTAGCATGAAAGTCCCACCTTGATTATTG
 TTATTGAAAACAGTATTCCAACTTTGTAAGTTGTTGATGTTTTGCTCCATGTAAC
 TTCTCCAGTGTCTGCATGAATTAGATTACTGCTGTCATTGTTATTCTTACCAA
 GTGCATTGATATGTGAAAGTAGAAATGCAAGGAAAGTTATGAAATATGGTGTGAGT
 TAGTAAAAGTGGCATTATTGGCTTATCTGCTCTATAGTTGTAAGATGAAAGTAA
 ACAAAATTGTTGACTATTAAATTATAGACCTTAAGCTGTTAGCAAGCATTAAA
 GCAAATGTATGGCTGCCATTGAAATATTGATGTTGCTGGCAGGATACTGCAAAGAAC
 ATGGTTTATTAAATTAAACAGTCACCTAAATGCCAGTTGCTGAAAAAATCTTATA
 AGGTTTACCCCTGATACGGAATTACACAGGTAGGGAGTTAGGGACAATAGTGTAGG
 TTATGGATGGAGGTGCGTACTAAATTGAAATAACGAGTAATAATCTTACTTGGTAGAGA
 TGGCCTTGCACAAAGTGAACCTGTTGGTTAAACTCATGAAAGTATGGGTTCACT
 GGAAATGTTGGAACTCTGAAGGATTAGACAAGGTTTGAAGGATAATCATGGGTTAGA
 AGGAAGTGTGAAAGTCACTTGAAGTTAGTTGGGAGCTTAAAGGGTAGATTACTGAG
 GCTGGCACATGGTGAACCTGTCATAAAATCTGGCTTGGACATATGCTGTGGTC
 CAGCACTGAGAGGCTAGTGAAGATTGCTGAGCCCAGAGCCAAAGGTTGCACTGAG
 CGTCACTGCACTCTAGCTGCACAGAGTAAGCCAAAAAAATATATATATTGAAATCAAGG
 AGGCAAAATTGACAGGGAGGAAGTAACTGCAAAACCACTAGGCTTGTAGTAGGTACTTAT
 ATAAAATCTAGTCCAGTTCTCTCATTTAAAAAAATGAAAGACACTGAAATAACAGACTTAAATA
 GCTCAGATAGCTAATTAGGAAATTCAAGTTGGCCAATAATGCACTCTCTGACATTAA
 AAATAATTCTATTCAAAATACATGCAATTGATTACACCTCATACTGTGATAATTAAATGT
 GATGTGGATTGCTGGTCCAGCATGACCCATAAACAGGTAGAAGAAATGATGGAATGTTT
 AGAATAAACTCCTGCTTATAGTAACTACAGTTCAAAAGATGTTAAATGCTTTGTAT
 TTACTGCCATGTAATTGAAATATAGATTATTGTAACCTTCAACCTGAAAATCAAGCAGT
 ATGAGAGTTAGTTATTGTATGTGCACTAGTGTCTAATGAAGCTTTAAAATCTACAATT
 TCTCTTAAAAATATTATTAAATGTGAATGGAATATAACAATTGCTTAATTCCCCAAC
 TTATTCTGTGTGAGACATTGTTACCCACAATTGAAATGGCTGTGTTTACCTCTAAATAA
 ATGAAATTCAAGGAAAAAA

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FIGURE 41

MGSVLGLCSMASWIPLCGSAPCLLCRCCPSGNNSTVTRLIYALFLLVGVCVACVMLIPGME
EQLNKIPGFCENEKGVVPCNILVGYKAVYRLCFGlamFYLLSLLMIKVKSSSDPRAAVHNG
FWFFKFAAAIAIIIGAFFIPEGTFTTVWFYVGMAGAFCFILIQLVLLIDFAHSWNESWVEKM
EEGNSRCWYAALLSATALNYLLSLVAIVLFFVYYTHPASCSENKAFISVNMLLCVGASVMSI
LPKIQESQPRSGLLQSSVITVYTMWTSAMTNEPETNCNPSLLSIIGYNTTSTVPKEGQSV
QWWHAQGIIGLILFLLCVFYSSIRTSNNSQVNKLTLTSDESTLIEDGGARSDGSLEDGDDVH
RAVDNERDGVTVSYSFFHFMLFLASLYIMMTLTNWSRYEPSREMKSQWTAVWVKISSSWIGI
VLYVWTLVAPLVLTNRDFD

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FIGURE 42

GCGAGAAAGAAGCTGTCTCCATCTTGTCTGTATCCCGCTGCTTCTTGNACGTTGTGGAGAT
GGGGAGCGTCCCTGGGGCTGTGCTCCATGGCGAGCTGGATACCATGTTGTGTGGAAGTGCC
CCGTGTTGCTATGCCGATGCTGCTCTAGTGGAAACAANTCCACTGTAACTAGATTGATCTA
TGCACCTTTCTTGCTTGGAGTATGTTAGCTTGTGTAATGTTGATACCAGGAATGGAAG
AACAACTGAATAAGATTCCCTGGATTTGTGAGAATGAGAAAGGTGTTGTCCTTGTAACATT
TTGGTTGGCTATAAAGCTGTATATCGTTGTGCTTGGCTATGTTCTATCTTCTTCT
CTCTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTGCACAATGGAT
TTGGTTCTTAAATTGCTGCAGCAATTGCAATTATTATTGGGGC

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FIGURE 43

GTTATTGTGAACCTTGTGGAGATGGGAGGTCNTGGGCTGTGTTCCATGGCGAGCTGGATAC
CANGTTGTGGAAGTGCCCGTGTGNTATGCCGATGCTGTCCTAGTGGAAACAANTCC
ACTGTAATTAGATTGATNTATGCACCTTNTTGCTTGGAGTANGTAGCTTGTGTAAT
GTTGATAACCAGGAATGGAAGAACAACTGAATAAGATTCTGGATTTGTGAGAATGAGAAAG
GTGTTGTCCCTGTAAACATTTGGTTGGCTATAAAGCTGTATATNGTTGTGCTTGTTG
GCTANGTTCTATNTTCTCTCTTTACTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAG
AGCTGCAGTGCACAATGGATTTGGTTTAAATTGCTGCAGCAATTGCAATTATTATTG
GGGC

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FIGURE 44

AAGAAGCTGTCATCTTGTCTGTATCCGCTGCTCTGTAAACGTTNTGGAGATGGGAGC
GTCCTGGGGTTGTGCTCCATGGCGAGCTGGATACCATGTTGTGGAAGTGCCCCGTGTT
TGCTATGCCGATGCTGCTAGTGGAAACAACCTCCACTGTAACTAGATTGATCTATGCACCT
TTCTTGCTTGGAGTATGTAGCTTGTGTAATGTTGATACCAGGAATGGAAGAACAACT
GAATAAGATTCCCTGGATTTGTGAGAATGAGAAAGGTGTTGTCCCTTGTAAACATTTGGTTG
GCTATAAAGCTGTATATCGTTGTGCTTGGTTGGCTATGTTCTATCTTCTCTTTA
CTAATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTCACAATGGATTTGGTT
CTTAAATTGCTGCAGCAATTGCAATTATTATTGGGGC

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FIGURE 45

GCTGTCCTTAGTGGAAACAANTCCAACCTGTAACCTGGATTGATCTATGCACTTTTCCTG
CTTGTGGAGTATGTAGCTTGTATAATGTTGTCAGGATTGGANGAACAACTGAATA
AGATTCTGGATTTGTGAGAATGAGAAAGGTGTTGTCCTGTAACATTTGGTTGGC
TATAAAGCTGTATATCGTTGTGCTTGGCTATGTTCTATCTTCTCTCTTACT
AATGATCAAAGTGAAGAGTAGCAGTGATCCTAGAGCTGCAGTCACAATGGATTTGGTTCT
TTAAATTGCTGCAGCAATTGCAATTATTATTGGGGCATTCTCATTCCAGAAGGAACCTT
ACAACGTGTTTATGTAGGCATGGCAGGTGCCTTGTTCATCCTCATACAACAGT
CTTACTTATTGATTTGCACATTGAAATGAATCGTGGGTTGAAAAAATGGAAGAAGGGA
ACTCGAGATGTTGGTATGCAGCCTGTTACAGCTACAGCTGAAATTATCTGCTGTCTTA
GTTGCTATCGTCCTGTTCTTGTCTACTACACTCATCCAGCCAGTGTTCAGAAAACAAGGC
GTTCATCAGTGTCAACATGCTCCTCTGCCTGGTGCCTGTAATG

FIGURE 46

CTCGGGCGCGCACAGGCAGCTCGGTTGCCCTCGGATGAGCTGCGGGTCGGGCCGCCGCTCTCCAAT
GGCAAATGTGTGTGGCTGGAGGGCAGCGCAGGGCTTCGGCAAAGGCAGTCGAGTGTGAGACCGGGCGAG
TCCTGTGAAAGCAGATAAAAGAAAACATTATTAACGTGTCATTACGAGGGAGCGCCGGCGGGCTGTCGC
ACTCCCCGCGAACATTGGCTCCCTCCAGCTCCGAGAGAGGAGAAGAAGAAGCGAAAAGAGGCAGATTAC
GTCGTTCCAGCCAAGTGGACCTGATGATGCCCTCTGAATTATCACGATATTGATTTAGCGATGCC
CCCTGGTTTGTGTTACGCACACACAGTCGACACAAGGCTCTGGCTGCTCCCTCCCTCGTTCCAGCTCC
TGGCGAATCCCACATCTGTTCAACTCTCCGCCGAGGGCGAGCAGGAGCGAGAGTGTGAGTGAATCTGCGAGTG
AAGAGGGACGAGGGAAAAGAAAACAGACGCAACTTGAGACTCCGCATCCAAAAGAAGACACCAGAT
CAGCAGGGAAAAGAAGATGGGCCCCCGAGGCTCTGCTGTGCTTGTGCCACTGTGTTCTCCCTGCTGG
TGGAAAGCTCGGCTTCTCTGTCGACCCACCGGCTGAAAGGCAGGTTTCAGAGGGACCGCAGGAACATCGGCC
ACATCATCTGGTGTGACGGACGACCAGGATGTGGAGCTGGGTTCCATGCGAGTGAACAAAGACCGGCGC
ATCATGGAGCAGGGGGCGCACTTCATCAACGCTCTGTCGACACACCCATGTCGCTGCCCTCACGCTCTC
CATCCTCATGGCAAGTACGTCCACAACACACCTACACCAACAATGAGAACGTGCTCTCGCCCTCTGG
AGGCACAGCACGAGAGCCGACCTTGCGGTGACCTCAATAGCACTGGCTACCGGACAGCTTCTCGGGAG
TATCTAATGAATACAACGGCTCTACGTGCCACCCGGCTGGAAGGAGTGGGTCGACTCTTAAAACCTCCG
CTTTTATAACTACACGCTGTGCGAACGGGTGAAAGAGAAGCAGGCTCCGACTACTCCAAGGATTACCTCA
CAGACCTCATACCAATGACAGCGTGAGCTCTCCGCACGTCCAAGAAGATGACCCGACAGGCCAGTCCTC
ATGGTCATCAGCCATGCAAGCCCCCACGGGCTGAGGATTCAAGCCCCACAATTACGCGCTCTTCCAAACGC
ATCTCAGCACATCACGCCAGCTACAACACTACGCGCCCAACCCGGACAAACACTGGATCATGCGTACACGGG
CCATGAAGCCCACATCACATGGAATTCAACACATGCTCCAGCGGAAGCGCTTGCAAGACCCCATGTCGTTGGAC
GACTCCATGGAGACGAGTATCACACATGCTGGTGTGAGACGGGCGAGCTGGACACACGTACATGTTACACCCG
CGGACACGGTTACACACATCGGCCAGTTGGCTGGTGAAGGGGAATCCATGCCATATGAGTTGACATCAGGG
TCCCCTTCTACGTGAGGGGCCCCAACGTTGGCTGGTGAAGGGGGCTGTCTGAATTCCACATCGCTTCAACATGACCTG
GCCGCCACCATCTGGACATTGCAAGGCCCTGGACATACCTGCGGATATGGACGGGAAATCCATCCTCAAGTGTCT
GGACACGGAGCGGCCGGTGAATGGTTCACTTGAAAAGAAGATGAGGGCTGGCGGACTCTTCTGGTGG
AGAGAGGCAAGCTGCTACACAAGAGAGACAATGACAAGGTGGACGCCAGGGAGAAGACTTCTGCCAAGTAC
CAGCGTGTGAAGGACCTGTCAGCGTGTGAGTACCAAGACGGCGTGTGAGCAGCTGGGACAGAAGTGGCAGTG
TGTGGAGGACGCCACGGGAAGCTGAAGCTGCATAAGTGCAGGGCCCCATGGGCTGGCGGAGCAGAGCCC
TCTCCAACTCTGTGCCAAGTACTACGGGAGGGCAGGCGAGGCCCTGCACCTGTGACAGGGGGACTACAAGCTC
AGCCTGGCGGAGCGGGAAAAACTCTCAAGAAGAAGTACAAGGCCAGCTATGTCGCTCCATCC
CTCAGTGGCCATCGAGGTGGACGCCAGGGTGTACACAGTAGGCCCTGGGTGATGCCGCCAGCCCCAACCTCA
CCAAGCGGCACTGGCCAGGGGCCCTGAGGACCAAGATGACAAGGATGGTGGGACTTCAGTGGCACTGGAGGC
CTTCCCAGACTACTCGGCCAACCCATTAAAGTGACACATCGGTGCTACATCCTAGACAACGACACAGTCCA
GTGTGACCTGGACCTGTACAAGTCCCTGCAAGGCTGGAAAGACCAAGCTGTCACATCGACCCAGAGATTGAAA
CCCTGCAAAATAAGAACCTGAGGGAAAGTCCAGGTCACTGAGAAGAAAAGCGGAGAAGAAGATGTC
TGTCAAAATAAGCTACGCTACACCCAGCACAAAGGCCCTCAAGCACAGAGGCTCCAGTCTGCATCTTCTAG
GAAGGGCTGCAAGAGAAGGCAAGGTGTGGCTGGCGGAGCAGAAGCGCAAGAAGAAACTCCGAAGCTGC
TCAAGCGCTGCAAGAACACGACACGTGCAAGCATGCCAGGCCCTGAGTGTCTACCCACGGACAACCAGCACTGG
CAGACGGCCCTTCTGGACACTGGGCCCTTCTGTGCGCTGCACAGGCCAACAAACACGTACTGGTCAT
GAGGACCATCAATGAGACTCACAATTCTCTGTAATTGCAACTGGCTCTAGAGTACTTGTATCTCA
ACACAGACCCCTACCGCTGATGAATGCACTGGACAGGGATGTCCTCAACCCAGCTACACGTACAG
CTCATGGAGCTGAGGAGCTGCAAGGGTACAAGCAGTGTAAACCCCGACTGAAACATGGACCTGGATGGAGG
AAGCTATGAGCAATAACAGGCAGTTCAAGCGTCAAGGAGAAGATGAAGAGACCTTCTCCAAATCACTGG
GACAACGTGGGAAGGCTGGGAAGGTTAAAGAAACACAGAGGTGGACCTCCAAAACATAGGGCATCACCTGA
CTGCACAGGCAATGAAAAACCATGTTGGCTGATTTCCAGCAGACCTGCTATGGCCAGGAGGCTGAGAAGC
AAGCACCGACTCTCAGTCAGTCACATGCAAGATCTGGAGGATAACCGAGCAGGAGAGATAACTCTAGGAAGTCC
ATTTTGGCCCTGCTTTGCTTGGATTATACCTCACAGCTGCAACAAAATGCAATTTCGTATCAAAAGTC
ACCAACTAACCTCCCCAGAACGTCACAAAGGAAAACGGAGAGGAGAGCAGGAGAGATAACTCTGGAAATTTC
TCCCAAGGGCGAAAGTCATTGGATTAAATCATAGGGGAAAGCAGTCCTGTTCTAAATCCTTATTCTT
TTGGTTTGTCAAAAGAAGGAACTAAGAAGCAGGACAGGGCAACGTGGAGAGGCTGAAAACAGTGCAGAGACG
TTGACAATGAGTCAGTAGCACAAGAGAGATGACATTACCTAGCACTATAAACCTGGTGTGCCCTGAGAAGAAA
CTGCCCTCATGTATATGTGACTATTACATGTAATCAACATGGAACTTTAGGGAAACCTAATAAGAAA
CCCAATTTCAGGAGTGGTGTCAATAAACGCTGTGGCCAGTGTAAAAGAAAAA

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FIGURE 47

MGPPSLVLCLLSATVFSLLGGSSAFLSHRLKGRFQRDRRNIRPNIILVLTDDQVELGSMQ
VMNKTRRIMEQGGAHFINAFVTPMCCPSRSSILTGKYVHNHNTYTNENCSSPSWQAQHES
RTFAVYLNSTGYRTAFFGKYLNEYNGSYVPPGWKEVGLLKNSRFYNYTLCRNGVKEKGSD
YSKDYLTDLITNDSVSFFRTSKKMYPHRPVLMVISHAAPHGPEDSAPQYSRLFPNASQHITP
SYNYAPNPDKHWIMRYTGPMPKPIHMEFTNMLQRKRLQTLMSVDDSMETIYNMLVETGELDNT
YIVYTADHGYHIGQFGLVKKGKSMPYEFDIRVPFYVRGPNEAGCLNPHIVLNIDLAPTILD
AGLDIPADMDGKSILKLLDTERPVNRFHLLKKMRVWRDSFLVERGKLLHKRDNDKVDAQEEN
FLPKYQRVKDLCQRAEYQTACEQLGQKWCEDATGKLKLHKCKGPMRLGGSRALSNLVPKY
YGQGSEACTCDSGDYKLSLAGRRKKLFKKYKASYVRSRSIRSVAIEVDGRVYHVGLDAAQ
PRNLTKRHWPAGAPEDQDDKDGGDFSGTGLPDYSAANPIKVTHRCYILENDTVQCDLDLYKS
LQAWKDHLHIDHEIETLQNKIKNLREVRGHLKKRPEECDCHKISYHTQHKGRLKHRGSSL
HPFRKGLQEKDVKVWLREQKRKKKLRKLLKRLQNNNTCSMPGLTCFTHDNQHWQTAPFWTLG
PFCACTSANNNTYWCMRTINETHNLFCEFATGFLEYFDLNTDPYQLMNAVNTLDRDVLNQL
HVQLMELRSCKGYKQCNPRTRNMDLDGGSYEQYRQFQRRKWPEMKRPSSKSLGQLWEGWEG

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FIGURE 48

AACAAAGTTCACTGACTGAGAGGGCTGAGCGGAGGCTGCTGAAGGGGAGAAAGGAGTGAGGA
GCTGCTGGGCAGAGAGGGACTGTCCGGCTCCAGATGCTGGCCTCCTGGGGAGCACAGCCC
TCGTGGATGGATCACAGGTGCTGCTGTGGCGGTCCCTGCTGCTGCTGCTGCTGGCCACC
TGCCTTTCCACGGACGGCAGGACTGTGACGTGGAGAGGAACCGTACAGCTGCAGGGGAAA
CCGAGTCCGCCGGGCCAGCCTGGCCCTTCCGGCGGCCACCTGGGAATCTTCACC
ATCACCGTCATCCTGCCACGTATCTCATGTGCCAATGTGGCCTCCACCACCAC
CCCCGCCACACCCCTACCAACCTCCACCACCAACCCCCACCGCCACCATCCCCGCCA
CGCTCGCTGGCTGCTGTCGCCGGTGCCTGTGGACAGCAGCTGCCCTGCCCTCCATCTG
TTCCCAAGGACAAGTGGACCCATGTTCCATGTGGAAGGATGCATCTCTGGGTGAACGAGG
GGAACAATAGACTGGGGCTTGCTCCAGCTGCATTGCATGGCATGCCCAAGTGTACTATGGC
AGCAGAGAAATGGAGGAACACTGGGTCTGCAGTGCTGAAGGGTTGGGAGTGGAGAGCAAGG
GTGCTTTGGGGCTGGACAGCCGTCTGTGACAGTGACTCCCAGTGAGCCCCAGAAATG
ACAAGCGTGTCTGGCAGGCCAGCACACAAGTGGATGTGAAGTGCCGTCTGACCTCCTC
ATCAGGCTGCTGCAGGCCCTGGCGGGCAGGGCACTGGGAGAGGCCCTGAGAATGTCCCTT
GGTTGGAGAAGGCAGTGTGAGGCTGCACAGTCATTGCGCTTAGTCCAAGAAAAT
AAAAACCACTAAGAAGCTTAAAAAAAAAAAAAAAAAAAAA

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FIGURE 49

MLGLLGSTALVGWITGAAVAVLLLLLLATCLFHGRQDCDVERNRTAAGGNVRRAQPWPFR
RRGHLGIFHHHRHPGHVSHVPNVGLHHHHHPRHTPHHLHHHHHPRHHPRHAR

FIGURE 50

GGCGGCTGCTGAGCTGCCTGAGGTGCAGTGTGGGGATCCAGAGCCATGTCGGACCTGCTA
CTACTGGGCCTGATTGGGGCCTGACTCTCTACTGCTGCTGACGCTGCTGGCCTTGCCGG
GTACTCAGGGCTACTGGCTGGGTGGAAGTGAGTGCTGGTCACCCCCATCCGCAACGTCA
CTGTGGCCTACAAGTCCACATGGGCTCTATGGTGAGACTGGCGGCTTTCACTGAGAGC
TGCAGCATCTCTCCCAAGCTCCGCTCCATCGCTGTCTACTATGACAACCCCCACATGGTGCC
CCCTGATAAGTGCCGATGTGCCGTGGCAGCATTGAGTGAAGGTGAGGAATGCCCTCCC
CTGAGCTATCGACCTTACCAAGAAATTGGCTCAAGGTGTTCTCCTCCGGCACCCAGC
CATGTGGTACAGCCACCTCCCTACACCACATTGTCCATCTGGCTGGCTACCCGCG
TGTCCATCCTGCCTGGACACCTACATCAAGGAGCGGAAGCTGTGTGCTATCCTCGGCTGG
AGATCTACCAGGAAGACCAGATCCATTGATGTGCCACTGGCACGGCAGGGAGACTTCTAT
GTGCCTGAGATGAAGGGAGACAGAGTGGAAATGGCGGGGGCTGTGGAGGCCATTGACACCCA
GGTGGATGGCACAGGAGCTGACACAATGAGTGACACGAGTTCTGTAAGCTTGGAAAGTGAGCC
CTGGCAGCCGGAGACTTCAGCTGCCACACTGTCACCTGGCGAGCAGCCGTGGCTGGGAT
GACGGTGACACCCGCAGCGAGCACAGCTACAGCGAGTCAGGTGCCAGCGGCTCCTTTGA
GGAGCTGGACTTGGAGGGCGAGGGGCCCTAGGGGAGTCACGGCTGGACCCCTGGACTGAGC
CCCTGGGACTACCAAGTGGCTCTGGAGGCCACTGCCCTGAGAAGGGCAAGGGTAACCC
ATGGCCTGCACCCCTCCTGCAGTGCAGTTGCTGAGGAACGTGAGCAGACTCTCCAGCAGACTCT
CCAGCCCTTCCTCCTCTGGGGAGGGGGTTCTGAGGGACCTGACTTCCCTGC
TCCAGGCCTTGTAAAGCCTCTCCTACTGCCCTTAGGCTCCAGGGCAGAGGAGCCA
GGGACTATTTCTGCACCAGCCCCAGGGCTGCCGCCCTGTTGTCTTTTCAGACTC
ACAGTGGAGCTTCCAGGACCCAGAATAAGCCAATGATTTACTTGTTCACCTGGAAAAAAA
AAAAAAAAAA

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FIGURE 51

MSDLLLGLIGGLTLLLLLTLAFAAGYSGLLAGVEVSAGSPPIRNVTVAYKFMGLYGETGR
LFTESCSISPRLRSIAVYYDNPHMVPDKRCRAVGSIILSEGEESPSPELIDLYQKFGFKVFS
FPAPSHVVTATFPYTTILSIWLATRRVHPALDTYIKERKLCAYPRLEIYQEDQIHFMCPALAR
QGDFYVPEMKETEWKWRGLVEAIDTQVDGTGADTMSDTSSVSLEVSPGSRETSAAATLSPGAS
SRGWDDGDTRSEHSYSESAGSSFEELDLEGEGPLGESRLDPGTEPLGTTKWLWEPTAPEK
GKE

FIGURE 52

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FIGURE 53

MTLRPSLLPLHLLLLLSSAVCRAEAGLETESPVRTLQVETLVEPPEPCAEPAAFGDTLHI
HYTGSLVDGRIIDTSILRDPLVIELGQKQVIPGLEQSLLDMCVGEKRRAIIPSHLAYGKRGF
PPSVPADAVVQYDVELIALIRANYWLKLVKGILPLVGMAMVPALLGLIGYHLYRKANRPKVS
KKKLKEEKRNKSKKK

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FIGURE 54

CCCGGGAACGTGTTCTGGCTGCCGCACCGAACAGCCTGTCCTGGTCCCCGGCTCCCTGC
CCCGCGCCCAGTCATGACCTGCGCCCTCACTCCTCCGCTCCATCTGCTGCTGCTGCTGC
TGCTCAGTGCAGCGGTGTGCCGGCTGAGGCTGGCTCGAAACCGAAAGTCCGTCGGACC
CTCCAAGTGGAGACCCCTGGTGGAGCCCCAGAACCATGTGCCGAGCCCGCTGCTTTGGAGA
CACGCTTCACATACACTACACGGGAAGCTGGTAGATGGACGTATTATTGACACCTCCCTGA
CCAGAGACCCCTGGTTATAGAACTTGGCAAAGCAGGTGATTCCAGGTCTGGAGCAGAGT
CTTCTCGACATGTGTGGAGAGAACGCAAGGGCAATCATTCCTCTCACTTGGCCTATGG
AAAACGGGGATTTCCACCATCTGTCCCAGCGGATGCAGTGGTAGTGCAGTGGAGCTGA
TTGCACTAATCCGAGCCAACTAAGCTGGCTAAAGCTGGTAGAGGGCATTGCCTCTGGTAGGG
ATGGCCATGGTGCCACCCCTGGCCTCATTGGGTATCACCTATACAGAAAGGCCAATAGA
CCCAAAGTCTCCAAAAAGAAGCTCAAGGAAGAGAAACGAAACAAGAGCAAAAGAAATAATA
AATAATAAATTTAAAAACTTA

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FIGURE 55

CCGAAAGTCCGTCCGGACCCTCCAAGTGGAGACCCCTGGTGGAGCCCCAGAACCATGTGCC
GAGCCCGCTGCTTGGAGACACGCTTCACATACACTACACGGGAAGCTGGTAGATGGACG
TATTATTGACACCTCCCTGACCAGAGACCCCTCTGGTTATAGAACTTGGCAAAGCAGGTGA
TTCCAGGTCTGGAGCAGAGTCTCTCGACATGTGTGGAGAGAAGCGAAGGGCAATCATT
CCTCTCACTTGGCCTATGGAAAACGGGGATTCCACCATCTGTCCCAGCGGATGCAGTGGT
GCAGTATGACGTGGAGCTGATTGCACTAATCCGAGCCAACACTGGCTAAAGCTGGTGAAGG
GCATTTGCCCTGGTAGGGATGCCATGGTGCCAGCCCTCCTGGGCCTCATTGGGTATCAC
CTATACAGAAAGGCCAATAGACCCAAAGTCTCCAAAAGAAGCTCAAGGAAGAGAAACGAAA
CAAGAGCAAAAGAAATAATAATAATAATTTAAAAAACTTAAAAA

FIGURE 56

CTGCTGCATCCGGGTGCTGGAGGCTGTGGCCGTTTGTCTGGCTAAATCGGGGGAG
TGAGGCAGGGCCGGCGCGCGACACCGGGCTCCGAACCACTGCACGACGGGGCTGGACTG
ACCTGAAAAAAATGTCTGGATTCTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGG
GAAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTACTATTTTACAGGCTGGTGGAT
TATCATAGATGCAGCTGTTATTATCCCACCATGAAAGATTCAACCACTCATACCATGCCT
GTGGTGTATAGCAACCATAGCCTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGA
GGTGATAGTTACAGTGAAGGTTGTCTGGGTCAAACAGGTGCTCGCATTGGCTTTGTTGG
TTTCATGTTGGCCTTGGATCTGATTGCATCTATGTGGATTCTTTGGAGGTTATGTTG
CTAAAGAAAAAGACATAGTATAACCTGGAATTGCTGTATTTCCAGAATGCCTCATCTT
TTTGGAGGGCTGGTTTAAGTTGGCCGACTGAAGACTTATGGCAGTGAACACATCTGAT
TTCCCACAGCACAACAGCCCTGCATGGTTGTTTTACTGCTCACTCCAACCTT
TTGTAATGCCATTTCTAAACTTATTCAGTGAGTGTAGTCAGCTAAAGTTGTGAATACT
AAAATCACGAGAACACCTAAACAACAAACAAAAATCTATTGTTGATGCACTTGATTAACCT
ATAAAATGTTAGAGGAAACTTCACATGAATAATTTGTCAAATTTATCATGGTATAATT
TGTAAAAATAAAAGAAATTACAAAAGAAATTATGGATTGTCAATGTAAGTATTGTCATA
TCTGAGGTCAAACACCACAATGAAAGTGCCTGAAAGATTAAATGTGTTATTCAAATGTGGT
CTCTTCTGTGTCAAATGTTAAATGAAATATAACATTAGTTTAAATATTCCGTGG
TCAAAATTCTCCTCACTATAATTGGTATTACTTTACCAAAATTCTGTGAACATGTAAT
GTAACCTGGCTTGAGGGTCTCCAAGGGGTGAGTGGACGTGTTGGAAGAGAGAAGCACCAC
GGTCCAGCCACCAGGCTCCCTGTGTCCCTCATGGGAAGGTCTCCGCTGTGCCTCTCATT
CCAAGGGCAGGAAGATGTGACTCAGCCATGACACGTGGTTCTGGTGGATGCACAGTCAC
CACATCCACCACTG

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FIGURE 57

MSGFLEGLRCSECIDWGEKRNTIASIAAGVLFFTGWIIIDAAVIYPTMKDFNHSYHACVI
ATIAFLMINAVSNGQVRGDSYSEGCLGQTGARIWLFVGFMLAFGSLIASMWILFGGYVAKEK
DIVYPGIAVFFQNAFIFFGGLVFKFGRTEDLWQ

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FIGURE 58

TTCTTGGCTAAAATCGGGGGAGTGAGGCAGGCGCGCGCGACACCGGGCTCCGGAACC
ACTGCACGACGGGGCTGGACTGACCTGAAAAAAATGTCTGGATTCTAGAGGGCTTGAGATG
CTCAGAATGCATTGACTGGGGGGAAAGCGCAATACTATTGCTTCCATTGCTGCTGGTGTAC
TATTTTTACAGGCTGGTGGATTATCATAGATGCAGCTGTTATTATCCCACCATGAAAGAT
TTCAACCACCTCATACCAGCCTGTGGTGTAGCAACCAGCCTCCTAATGATTAATGC
AGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTTGTCGGTCAAACAGGTG
CTCGCATTGGCTTTCGTTGGTTCATGTTGGCCTTGGATCTGATTGCATCTATGTGG
ATTCTTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTATAACCTGGAATTGCTGTATT
TTTCCAGAATGCCTTCATCTTTGGAGGGCTGGTTTAAGTTGGC

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FIGURE 59

TGGACGGACCTGAAAAAAATGTTGGATTNTAGAGGGNTTGAGATGTCAGAATGCATGAC
TGGGGAAAAGCGCAAATACTATTGCTTCCATTGCTGCTGGTANTATTTTACAGGCTG
GTGGATTATCATAGATGCAGNTGTTATTATCCACCATGAAAGATTCAACCANTCATACC
ATGCCTGTGGTGTATAGCAACCATAGCCTCNTAATGATTAATGCAGTATCGAATGGACAA
GTCCGAGGTGATAGTTACAGTGAAGGTTGGTCAACAGGTGCTCGCATTGGCTTT
CGTTGGTTCATGTTGGCCTTGGATCTCTGATTGCATCTATGTGGATTCTTTGGAGGTT
ATGTTGCTAAAGAAAAAGACATAGTATAACCTGGAATTGNTGTATTTTCCAGAATGCCTTC
ATCTTTTGGAGGGCTGGTTTAAGTTGGCCGCACTGAAGANTTATGGCAGTG

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FIGURE 60

GGACACCGGGTTCCGGACCAATGCANGACGGGTGGANTGACCTGAAAAAAATGTTGGATT
TTTAGAGGGCTTGAGATGNTCAGAATGCATTGACTGGGGAAAAGCGCAATANTATTGCTTT
CCATTGCTGCTGGTGTACTATTTTACAGGGTGGTGGATTATCATAGATGCAGCTGTTATT
TATCCCACCATGAAAGATTNAACCACTCATACCATGCCTGTGGTGTATAGCAACCATAGC
CTTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTT
GTTTGGGTCAAACAGGTGNTCGCATTGGCTTTCGTTGGTTCATGTTGGCCTTGGATT
CTGATTGNATTCTATGC GGATTCTTCTTGGAGGTTATGTTGCTAAAGAAAAAGACATAGTAT
ACCCTGGAATTNCTNTATTTCCAGAATGCC

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FIGURE 61

TAGAGGGCTTGAGATGCTCAGAACATGCATTGACTGGGGGAAAAGCGCAATANTATTGCTTCC
ATTGNTGNTGGTGTANTATTTTACAGGCTGGTGGATTATNATAGATGCAGCTGTTATTT
ATCCCACCATGAAAGATTTNAACCANTCATACCATGCCTGTGGTGTATAGCAACCATAGCC
TTCCTAATGATTAATGCAGTATNGAATGGACAAGTCCGAGGTGATAGTTACAGTGAAGGTG
TTTGGGTCAAACAGGTGNTNGCATTGGCTTTNGTTGGTTCATGTTGGCCTTGGATCTN
TGATTGCATTTATGTGGATTNTTTGGAGGTTATGTTGCTAAAGNAAAAGACATAGTATAC
CCTGT

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FIGURE 62

GGGAGGGCTGTGNCCGTTTGTGCTAAATGGGGAGTGAGGCGGCCGGCGCG
CGNGACACCGGGTCCGGAAACCATTGCACGACGGGTGGACTGACCTGAAAAAAATGTTG
GATTNTAGAGGGCTTGAGATGCTCAGAATGCATTGACTGGGGGAAAAGCGCAATACTATT
GCTTCCATTGCTGCTGGTGTACTATTTTACAGGCTGGTGGATTATCATAGATGCAGCTGT
TATTTATCCACCATGAAAGATTCAACCACTCATACCATGCCTGTGGTGTATAGCAACCA
TAGCCTCCTAATGATTAATGCAGTATCGAATGGACAAGTCCGAGGTGATAGTTACAGTGAA
GGTTGTCTGGGTCAAACAGGTGCTCGCATTGGCTTTCGTTGGTTCATGTTGCCCTTGG
ATNTCTGATTGCATCTATGTGGATTCTTTGGAGGTTATGTTGCTAAAGAAAAGACATAG
TATACCTGGAATTGCTGTATTTCCAGAATGCCTTCATNTTTGGAGGGCTG

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FIGURE 63

CGACGCCGGCGT**ATG**TGGCTTCCGCTGGTGTGCTCCTGGCTGTGCTGCTGGCGTCC
TCTGCAAAGTTACTTGGGACTATTCTCTGGCAGCTCCCCGAATCCTTCTCCGAAGATGTC
AAACGGCCCCCAGCGCCCTGGTAACTGACAAGGAGGCCAGGAAGAAGGTTCTCAAACAAGC
TTTCAGCCAACCAAGTGCCGGAGAAGCTGGATGTGGTGTAAATTGGCAGTGGCTTGGGG
GCCTGGCTGCAGCTGCAATTCTAGCTAAAGCTGGCAAGCGAGTCCTGGTGTGGAAACAACAT
ACCAAGGCAGGGGCTGCTGTACACCTTGGAAAGAATGGCCTTGAATTGACACAGGAAT
CCATTACATGGCGTATGGAAGAGGGCAGCATTGGCGTTTATCTTGGACCAGATCACTG
AAGGGCAGCTGGACTGGGCTCCCTGTCTCTCTTGCATCATGGTACTGGAAAGGGCC
AATGGCGAAAGGAGTACCCCATGTACAGTGGAGAGAAAGCCTACATTCAAGGGCCTCAAGGA
GAAGTTCCACAGGAGGAAGCTATCATTGACAAGTATAAAAGCTGGTTAAGGTGGTATCA
GTGGAGGCCCTCATGCCATCCTGTTGAAATTCTCCATTGGCGTGGTTCAAGCTCCTCGAC
AGGTGTGGGCTGCTGACTCGTTCTCCATTCTCAAGCATCCACCCAGAGCCTGGCTGA
GGTCTGCAGCAGCTGGGGCCTCCTCTGAGCTCCAGGCAGTACTCAGCTACATCTCCCCA
CTTACGGTGTCAACCCCAACACAGTGCCTTCCATGCACGCCGTGGTCAACCAACTAC
ATGAAAGGAGGCTTTATCCCCGAGGGGTTCCAGTGAATTCACACCATCCCTGT
GATTCAAGCAGGGCTGGGGCGCTGTCTCACAAAGGCCACTGTGCAGAGTGTGCTGGACT
CAGCTGGGAAAGCCTGTGGTGTCAAGTGTGAAGAAGGGGATGAGCTGGTGAACATCTATTG
CCCATCGTGGTCTCCAAACGCAGGACTGTCAACACCTATGAAACACCTACTGCCGGGGAACGC
CCGCTGCCAGGTGTGAAGCAGCAACTGGGAGCGGTGCGGGGGCTTAGGCATGACCT
CTGTTTCATCTGCCCTGCGAGGCACCAAGGAAGACCTGCATCTGCCGTCCACCAACTACTAT
GTTACTATGACACGGACATGGACCAAGGCAGTGGAGCGTACGTCTCCATGCCAGGGAAAGA
GGCTGCGAACACATCCCTCTTCTCTTCCATCAGCAAAGATCCGACCTGG
AGGACCGATTCCAGGCCGGTCCACCATGATCATGCTCATACCCACTGCCAACGAGTGGTT
GAGGAGTGGCAGGCAGCTGAAGGGAAAGCGGGCAGTGAACATGAGACCTTCAAAACCTC
CTTGTGGAAGCCTCATGTCACTGGTCTGAAACTGTTCCACAGCTGGAGGGAAAGGTGG
AGAGTGTGACTCGAGGATCCCCACTCACCAACCGATTCTATCTGGCTGCTCCCCAGGGTGC
TGCTACGGGCTGACCATGACCTGGGCGCTGCACCCCTGTGTGATGGCCTCCTTGAGGGC
CCAGAGCCCCATCCCCAACCTCTATCTGACAGGCCAGGATATCTCACCTGTGGACTGGTC
GGGCCCTGCAAGGTGCCCTGCTGTGCAGCAGGCCATCCTGAAGCGAACCTGTACTCAGAC
CTTAAGAATCTGATTCTAGGATCCGGCACAGAAAGAAAAAGAATT**ATG**TCCATCAGGGAGG
AGTCAGAGGAATTGCCAATGGCTGGGCATCTCCCTGACTTACCCATAATGTCTTC
CATTAGTTCTGCACGTATAAAGCACTTAATTGGTTCTGATGCCTGAAGAGAGGCC
TTAAATACAATTCCAATCTGGGCAATGGAATCACTGCCTCCAGCTGGGCAGGTGAGA
TCTTACGCCTTTATAACATGCCATCCCTACTAATAGGATATTGACTTGGATAGCTTGATG
TCTCATGACGAGCGGGCCTCTGCATCCCTCACCCATGCCCTAACTCAGTGTCAAGCGA
ATATTCCATCTGTGGATAGAACCCCTGGCAGTGTGTCACTGGCTTGGGTTCAAGTTC
TGTCCTGAGGCTTCTGCTCTCATTCAATTAGTGTCACTGCACAGTTCTACACTGTCAAGG
GAAAAGGGAGACTAATGAGGCTTAACCTAAAACCTGGGCGTGGTTTGGTGCACATTCCATA
GGTTTGGAGAGCTCTAGATCTTTGTCTGGGTTCACTGGCTCTCAGGGGACAGGAAAT
GCCTGTGTCTGGCAGTGTGGTTCTGGAGCTTGGGTTAACAGCAGGATCCATCAGTTAGTA
GGGTGCATGTCAGATGATCATATCCAATTCAATATGGAAGTCCGGGTCTGTCTCCATTATCA
TCGGGGTGGCAGCTGGTTCTCAATGTGCCAGCAGGGACTCAGTACCTGAGCCTCAATCAAGC
CTTATCCACCAAATACAGGGAAAGGGTGTGCAAGGGAGGGTACAGGAGTCAGGGCA
TGGACTGGTAAGATGAATACTTGCTGGGCTGAAGCAGGCTGCAGGGCATTCCAGCCAAGGG
CACAGCAGGGAGACTGTCAGGGAGGTGTGGGTAAGGGAGGGAAAGTCACATCAGAAAAGGG
AAGCCACGGAATGTGTGAAGCCCAGAAATGGCATTGCAAGTTGGAAAAATGACTTT
TTAGACAGGTAGGTGAATGCAAGCTCAAGGTTGGAAAAATGACTTTCACTGTTATGTCTTG
GTATCAGACATACGAAAGGTCTTTGTAGTTGTTAATGTAACATTAATAAAATTATTG
ATTCCATTGCTTAAAAAA

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FIGURE 64

MWLPLVLLAVLLAVLCKVYLGLFSGSSPNPFSEDVKRPPAPLVTDEARKVVKQAFSAN
QVPEKLDVVVIGSGFGLAAAAILAKAGKRVLVLEQHTKAGGCCHTFGKNGLEFDTGIHYIG
RMEEGSIGRFILDQITEGQLDWAPLSSPFDIMVLEGPNGRKEYPMYSGEKAYIQGLKEKFPQ
EEAIIDKYIKLVKVSSGAPHAILLKFLPLPVVQLLDRCGLLRFSPFLQASTQSLAEVLQQ
LGASSELQAVLSYIFFPTYGVTPNHSAFSMHALLVNHYMKGGFYPRGGSSEIAFHТИPVIQRA
GGAVLTKATVQSVLLDSAGKACGVSVKGHELVNICYCPIVVSNAGLFNTYEHLLPGNARCLP
GVKQQLGTVRPGLGMTSVFICLRGTKEDELHLPSTNYYVYYDTDMDQAMERYVSMPREEAAEH
IPLLFFAFPSAKDPTWEDRFPGRSTMIMLIPTAYEWFEWQAEKGKRGSDYETFKNSFVEA
SMSVVLKLFQLEGKVESVTAGSPLTNQFYLAAPRGACYGADHDLGRLHPCVMASLRAQSPI
PNLYLTGQDIFTCGLVGALQGALLCSSAILKRNLYSDLKNLDSRIRAQKKKN

FIGURE 65

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FIGURE 66

MRVRIGLTLCAVLLSLASASSDEEGSQDESLDSTTLTSDESVKDHTAGR VVAGQI FLD
SEESELESSIQEEEDSLKSQEGESVTEDISFLESPNPNKDYEPPKKVRKPALTAIEGTAHG
EPCHFPFLFLDKEYDECTS DGRDGRLWCATTYDYKADEKWGFCETEEEAKRRQM QEAEMM
YQTGMKILNGSNKKSQKREAYRYLQKAASMNHTKALERVSYALLFGDYL PQNIQAAREMFEK
LTEEGSPKGQTALGFLYASGLGVNSSQAKALVYYTGFALGGNLIAHMVLVSRL

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FIGURE 67

CTTCCCAGCCCTGTGCCCAAAGCACCTGGAGCATATGCCTGCAGAACTTCTACTGCCT
GCCTCCCTGCCTCTGGCCATGGCCTGCCGGTGCCTCAGCTCCTCTGATGGGACCTCCT
GTCAGTTCCCAGACAGTCCTGGCCAGCTGGATGCAGTCAGCTGGTCTTCCCAGGCCAAGTGG
CTCAACTCTCCTGCACGCTCAGCCCCAGCACGTACCATCAGGGACTACGGTGTGTCCTGG
TACCAGCAGCGGGCAGGCAGTGCCCCTCGATATCTCCTCTACTACCGCTCGGAGGAGGATCA
CCACCGGCCTGCTGACATCCCCGATCGATTCTCGGCAGCCAAGGATGAGGCCACAATGCCT
GTGTCCTCACCAATTAGTCCCCTGCAGCCTGAAGACGACGCCGGATTACTACTGCTCTGTTGGC
TACGGCTTAGTCCCTAGGGTGGGTGTGAGATGGGTGCCTCCCTCTGCCTCCCATTCT
GCCCTGACCTGGTCCCTTTAAACTTCTTGAGCCTGCTCCCTCTGTAAAATGGG
TTAATAATATTCAACATGTCAACAAAC

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FIGURE 68

MACRCLSFLLMGTFLSVSQTVLAQLDALLVFPQVAQLSCTLSPQHVTIRDYGVSWYQQRAG
SAPRYLLYYRSEEDHHRPADIPDRFSAAKDEAHNACVLTISPQPEDDADYYCSVGYGFSP

FIGURE 69

GCCGCCCCGCCCGAGACCGGGCCCAGGGGGCGCGGGGGCGGGATGCGGCGCCCGGGCGG
 CGATGACCGCGGAGCGCACGCCCGGGCCCGCCCTGACCCCGCCCGCCCGCTGAGCCC
 CCCGCCGAGGTCCGGACAGGCCGAG**ATG**ACGCCGAGCCCCCTGTTGCTGCTCCTGCTGCCGC
 CGCTGCTGCTGGGGCCTTCCCACCGGCCGCCGCCGAGGCCAAAGATGGCGGAC
 AAGGTGGTCCCACGGCAGGTGGCCGGCTGGGCCACTGTGCGGGCTGCAAGTGCCAGTGG
 GGGGGACCCGCCGCCGCTGACCATGTGGACCAAGGATGGCCGACCATCCACAGCGGCTGGA
 GCCGCTTCCCGTGTGCCGCAGGGCTGAAGGTGAAGCAGGTGGAGCGGGAGGATGCCGGC
 GTGTACGTGTCAAGGCCACCAACGGCTCGGCAGCCTGAGCGTCAACTACACCCCTCGTCGT
 GCTGGATGACATTAGCCCAGGGAGAGGAGACGCCACTGGGCCACAGCTCTCTGGGGGTCAG
 AGGACCCGCCAGCCAGCAGTGGGACACGCCGCTCACACAGGCCAAAGATGAGGCC
 CGGGTGTATGCCACGGCCCGTGGGTAGCTCGTGCCTCAAGTGCCTGGCCAGCGGGCACCC
 TCGGCCGCACATCACGGTGGATGAAAGGACGACCCAGGCCCTGACGCCAGAGGCCGCTGAGC
 CCAGGAAGAAGAAGTGGACACTGAGCTGAAGAACCTGCGCCGGAGGACAGCGGAAATAC
 ACCTGCCGCGTGTGAAACCGCGGGGCCATCAACGCCACTACAAGGTGGATGTGATCCA
 GCGGACCCGTTCCAAGCCCCTGCTCACAGGCACGCACCCGTGAACACGACGGTGGACTTCG
 GGGGGACACAGTCCTTCAGTGCAGGTGCGCAGCGACGTGAAGGCCGGTGTATCCAGTGGCTG
 AACGCGTGGAGTACGGCGCCAGGGCCACAACACTCCACATCGATGTGGCGGCCAGAA
 GTTTGTGGTGTGCCCCACGGGTGACGTGTTGCGCCGACGGCTCTACCTCAATAAGC
 TGCTCATCACCGTGGCCGCCAGGACATGCGGGCATGTACATTCGCTTGGCGCCAAACACC
 ATGGGCTACACGCTTCCCGCAGGCCCTTCCCTCACCGTGTGGCCAGACCCAAAACGCCAGGGCC
 ACCTGTGGCTCCTCGTCTCGCCACTAGCCTGCCGTGGCGCTGGTATCGGCATCCAG
 CCGCGCTGTCTCATCCTGGCACCCCTGCTCTGGCTGGCCAGGCCCCAGAAGACCG
 TGCACCCCCCGCGCTGCCCTCCCCCTGCTGGGACCCGCCGGGACGGCCGCGACCG
 CAGCGGAGACAAGGACCTTCCCTCGTTGCCGCCCTCAGCGCTGCCCTGGTGTGGGCTGT
 GTGAGGAGCATGGTCTCCGGCAGCCCCCAGCACTTACTGGGCCAGGGCCAGTTGCTG
 CCTAAGTTGACCCAAACTCTACACAGACATCCACACACACACACACACTCTCACAC
 ACACACTCACAGTGGAGGGCAAGGTCCCACAGCACATCCACTATCAGTGT**TAG**ACGGCACCGT
 ATCTGCAGTGGGACGGGGACGGGACATGGCAGGGAGAATGGCAGCACCCAGGCAGTCTGTG
 GCAGACGAAGGACGGGGACGGGACATGGCAGGGAGAATGGCAGCACCCAGGCAGTCTGTG
 TGAGGCATAGCCCCCTGGACACACACACAGACACACACTACCTGGATGCAATGTGAC
 ACACATGCGCGCACACGTGCTCCCTGAAGGCACACAGTACGCACACGCACATGCACAGATATG
 CCGCCTGGGCACACAGATAAGTGCACGCACACGCACAGAGACATGCCAGAAC
 TACAAGGACATGCTGCTGAACATACACACGCACACCATGCGCAGATGTGCTGCCCTGGACA
 CACACACACACGGATATGCTGCTGGACGCACACACGTGCAAGATATGGTATCCGGACACA
 CACGTGCACAGATATGCTGCTGGACACACAGATAATGCTGCTTGCACACACACATGCA
 ATATTGCTGGACACACACACACACACACACACACACACACACACACACACAC
 ACATGCAGATATGCTGCTGGACACACACTTCCAGACACACAGTGCACAGGCGCAGATATG
 GCCTGGACACACGCAGATATGCTGCTGGACACACACACGCACACGCAGACATGCTGCC
 ACACACACAGATAATGCTGCTCAACACACTCACACACAGTGCAGATATTGCTGGACACAC
 TGTGCACAGATATGCTGCTGGACATGCAACACACAGTGCAGATATGCTGCTGGGACACAC
 CACGCACACATGCAGATATGCTGCTGGGACACACACTTCCGGACACACATGCACACACAG
 GCAGATATGCTGCTGGACACACACAGATAATGCTGCTCAACACACTCACACACGTG
 TATTGCTGGACACACACATGTCACAGATAATGCTGCTGGACATGCAACACACAGTGCAGATA
 TGCTGCTGGGATACACACAGCAGCACACACATGCAAGATATGCTGCTGGGACACACACTTCC
 CACACATGCACACACACAGGTGCAGATATGCTGCTGGACACACAGCAGACTGACGTG
 TTTGGGTTGCGCTGAAAGCCTGCAGTACGTGTGCCGTGAGGCTCATAGTTGATGAGGGACTT
 CCCTGCTCACCGTCACTCCCCAACTCTGCCGCCCTGTCCCCGCCCTAGTCCCCGCC
 CATCCCCGCCCTGTCCCCCTGGCCTTGGGGCTATTTGCAACCTGCTTGGGTC
 AGTCCCCACTGCTGTGGCTGGGTTGGGGTGGGGCACAGCAGCCCCAAGCCTGAGAGGGCTGGAG
 CCCATGGCTAGTGGCTCATCCCCAGTGCATTCTCCCCCTGACACAGAGAAGGGCCTGGTA
 TTTATTTAAGAAATGAAGATAATAATTAATGATGGAAGGAAGACTGGGTTGCA
 TGTGGTCTCCTGGGGCCGGGACCCGCTGGCTTTCAAGCCATGCTGATGACCACAC
 GTCCAGGCCAGACACCACCCCCCAGGACTGTGCTGGTGGGCCAGATCTGT
 TGTAGAGTTGAGCTGAAGCCCCGTATTTAATTGTTAAACACAAAA

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FIGURE 70

MTPSPLLLLLPPLLGAFPPAAAARGPPKMADKVVPRQVARLGRTVRLQCPVEGDPPPLTM
WTKDRTIHSGWSRFRVLPQGLKVQVEREDAGVYVCKATNGFGSLSVNYTLVVLDDISPGK
ESLGPDSSSGQEDPASQQWARPRFTQPSKMRRVIARPVGSSVRLKCVASGHPRPDITWMK
DDQALTRPEAAEPRKKWTLSLKNLRPEDSGKYTCRVSNRAGAINATYKVDVIQRTRSKPVL
TGTHPVNTTVDFGGTTSFQCKVRSVDVKPVIQWLKRVEYGAEGRHNSTIDVGGQKFVVLPTGD
VWSRPDGSYLNKLLITRARQDDAGMYICLGANTMGYSFRSAFLTLPDPKPPGPPVASSSSA
TSLPWVIVIGIPAGAVFILGTLLWLCQAQKKPCTPAPAPPLPGHRPPGTARDRSGDKDLP
LAALSAGPGVGLCEEHGSPAAPQHLLGPGPVAGPKLYPKLYTDIHTHTHSHTHVEGKV
HQHIHYQC

FIGURE 71

CCAGCTGAGGAGCCCTGCTCAAGACACGGTCACTGGATCTGAGAAACTTCCAGGGACCGCATTCCAGAGTC
 AGTGAACCTGTGAAGCACCCACATCTACCTTGTCCACGGCTGGGGAAAGAATGGTGGGGACCA
 AGGCTGGGTGTTCTCTTCTGGTCTGGAAAGTCACATCTGTGTTGGGGAGACAGACGATGCTACCCAGTCA
 GTAAGAAGAGTCCAGCTGGAAAGAAGACCCACATCTGGCAAGCTGCGCAGACCCCTGGAGAGCCCTGG
 TGAGTGGACAAACATGGTCAACATCGACTTGTGAGGGCTGGGCAACTATGAGCCGGCTGGACGCCATTGCT
 TCTACTATGGGGACCGTGTATGTGCCGTCCCCCTGGCTAGAGGCTGGACCACTGACTGGACACCTGCGGC
 AGCACTGGCCAGGTGGTCATGGTAGTCCCCGTGAGGGTTCTGGTGCCTCAACAGGGAGCAGCGGCTGGCCA
 GAACGTCTAATTACCGTACGCTCTCTGCCCCACAGGATCTCTGCGCAGAGCACAGAGCGCATTGGA
 GCCCATGGTCTCTGGAGCAAGTGTCTGAGCTGGCTGAGCTGGGCTCAGACTGGGCTCAGACTCGCACACGCATTG
 TTGGCAGAGATGGTGTGCTGTGAGGCGAGCAAGAGGGTCACTGACTGATGCCCATGTGCCAGGACTGTACAGC
 CTGTGACCTGACCTGCCAATGGGCCAGGTGAATGCTGACTGTGATGCCCATGTGCCAGGACTCATGCTTC
 ATGGGGCTGTCTCTTCCCGAGGTGCCAGGCTGGGCTGATCTACCTCTGACCAAGACGCCAGGAG
 CTGCTGACCCAGACAGACAGTGTGGAGATTCCGATCTCTGGCTGTGCCCTGATGGCAAAGCATTCTGAA
 GATCACAAAGGTCAAGTTGCCCATTTGACTCACAATGCCAAGACTAGCCTGAAGGCAGGCCACATCAAGG
 CAGAGTTGTGAGGGCAGAGACTCCATACATGGTGTGAACCCCTGAGACAAAAGCACGGAGAGCTGGCAGAGC
 GTGCTCTGTGCTGTGAAGGCCACAGGGAAAGCCAGGGCAGACAAAGTATTGGTGTATCATAATGACACATTG
 GGATCCTTCTCTACAAAGCATGAGAGCAAGCTGGTGTGAGGAAACTGCAAGCAGCACCCAGGCTGGGAGTACT
 TTGCAAGGCCAGAGTGTGCTGGGCTGTGAAGTCCAAGGTTGCCAGCTGATTGTCACAGCATCTGATGAG
 ACTCTTGTCAACCCAGTCTCTGAGAGCTATCTATCCGGTCTGCCCATGATTGCTTCAAGATGCCACCAACTC
 CTTCTACTATGAGCTGGGAGCTGCCCTGTTAAGACTGTGAGGGCAGCAGGATAATGGGATCAGGTGCCGTG
 ATGCTGTGAGAACTGCTGTGCTCATCTAACAGACAGAGGAAAGGGAGATCTGAGCTGGCTACACGCTACCC
 ACCAAGGTGGCCAAGGAGTGCAGCTGCCAGCGGTGTACGGAACACTGGAGCATGTGCCGGGCGGTGAGTGC
 TGCTGACAATGGGGAGCCATGCGCTTGGCATGTGATCTGGGAAACAGCGCTGTAAAGCATGACTGGCTACA
 AGGGCACTTCCCTCATGCCCCAGGACACTGAGAGGTGGTCTCACATTGTCAGGCTGAGAAG
 TTTGCAACACCAAAAGTGTACCTTCAACAAAGAAGGGAGTGGCTGTTCAICAAATCAAGATGCTTC
 TCGGAAAGAGCCATCACTTGGAAAGGCATGGAGACCAACATCATCCCCCTGGGGAAAGTGGTTGGTGAAGACC
 CCATGGCTGAACGGAGATCCATCAGGAGTTCTACAGGAGCAATGGGGAGCCCTACATAGGAAAAGTGAAG
 GCGAGTGTGACCTTCTGGATCCCCGAAATATTCCACAGGCCACAGCTGCCAGACTGACCTGAACCTCATCAA
 TGACGAAGGAGACACTTCCCCCTCGGACGTATGGCATGTTCTGTGACTTCAGAGATGAGGTACACCTCAG
 AGCAACTTAATGCTGGCAAAGTGAAGGTCCACCTGACTGACGCCAGGTCAAGATGCCAGACATATCCACA
 GTGAAACTCTGGTCACTCAATCCAGACACAGGCTGTGGGAGGGAGGAAAGGTGATTCAAATTTGAAAATCAAAG
 GAGGAACAAAAGAGAAGACAGAAACCTCTGGTGGCAACCTGGAGATTGTGAGGAGGCTCTTAACCTGG
 ATGTTCTGAAAGCAGCGGTGTTGGTAAGGTGAGGGCTACCGGAGTGTGAGGGTCTTGCCCTAGTGAAGCAG
 ATCCAGGGGGTGTGATCTCCGATTAACCTGGAGCTAGAACACTGGCTCTTGTCACCCCTAGGGCTGGGG
 CCGCTTGCAGCTGTACACAGGCCAACAGGGGCTGTGCTGCCCTCTGTGATGACAGTCCCCTGATG
 CCTACTCTGCCATGTCTGGCAAGCCTGGCTGGGAGGAACGTCAAGCAGTGGAGTCTCTCTAAATTCAAC
 CCAAATGCAATGGCGTCCCTCAGCCCTATCTCAACAAGCTCAACTACCGTCCGGACGGACATGAGGATCCACG
 GGTAAAAGAGCAGCTTCAGGATGGCATGGCAAGGCCAGGGCTACAGTGGAGGAGGAGCAATGGGCCA
 TCTATGCCCTGGAGAACCTGGGCGATGTGAAGAGGCCACCCAGTGCAGCCACTCCGGTTCTACCAGATT
 GAGGGGGATGATGACTACAACACAGTCCCCCTCAACGAAGATGCCATTGAGCTGGACTGAAGACTATCT
 GGCATGGTGGCCAAGGCCAGTGGAAATCAGGGCTGCTATGCAAGGTGAAGATTGTTGGGCCACTGGAAAGTGA
 ATGTCGATCCGCAACATGGGGGCACTCATGGCGGAGCAGTGGGAGGAGCTGATGGAATCCGAGATGTGAGG
 AGCACTCGGGACAGGGACCCAGGCCAACTGTCTCAGCTGCCCTGTGAGGTATCCCCCAGGGCAGCTGCCGTGAGGCCAGT
 TCAGGACCGTGTGGACCGCACCTGGTAAGGTATCCCCCAGGGCAGCTGCCGTGAGGCCAGTGTGAACCCCA
 TGCTGAGTGTGACCTGGTCAACACTGGCACTGCACTGACAGCACCCAGTGTGAGTACACCATGCTGGCA
 CCCCTGGGCCACCTGGGCAACAACTGGCATCTGGCAACTATGGCATCTACACTGCACTGACCCAGGACCTGCCAGGGGAGGAG
 CGCGCTCGGGCGGTGCTTGATGGCACATCGGATGGCTCTCCAGAATCATGAAGAGCAATGTGGAGTAGGCC
 TCACCTTCACACTGTGTAGAGAGGCAAGTAGGCCAGACTGCCCTGGAGGAGGAGCAGCAGCAGGAGCAGGGGTGGCCAGCG
 TCCAGGGTGGAGGTGGCCTCTGTGAGATTCTCAAGGTTCTGAGGTGCTCAACAGGCCCTGATCAACTAAGTTTG
 ACTTCACCCCTCTGCCCCATTTGATGTGACAGCCATTGAGACTGATGACAAACTGTCACCTGGTTAAT
 TTAAGCACTCTGTTTCTGTAATTGCTGTTGTTCTCATGCCCTTACTTACTTGTCCATGCTACTG
 TTGGCAGCTGGGCCCCCACAATGGCACAATAAAGCCCTTGTGAAACTGTTCTTTAAATGAAACACAAGAAAATT
 GGCACACTGGTAAACACTGTGAGCTCAACTGTACTTCAATTAAATGCCATTAAATGCAAAATATAACTTCTCTT
 TTGCACTGGTTTGCCCACCTCTGCAATAGTGTAAATCTGATGCTGAAGATCAAATAACCAATATAAAAGCATAT
 TTCTGGCCTTGCTCCACAGGACATAGGCAAGCCTGATCATAGTTCATACATATAATGGTGGTGAAGATAAAG
 AAATAAAACACAATAACTTTACTGAAATGAAATAACTTATTTCTGCTAAATTGGAAATTCTAGTGC
 ACATTCAAAGTAAAGCTTAAATATAAGGGTGTACATGTTCTACCAAGTGTGAAAGAACATCTCTG
 ATCCACAATTACACCAGGTGCTAAGTGTATTTGACATTTCCCTTGCATTGCTTTGCTTGTAGAAAC
 CCAGTGTAGGCCAGGGCAGATGTCAATAATGCATACTGTATTCGAAAAAA

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FIGURE 72

MVGTKAWVFSFLVLETSVLGRQTMLTQS VRRVQPGKKNPSIFAKP ADTLESPGEWTTWFNI
DYPGGKGDYERLDAIRFY YGDRVCARPLRLEARTTDWT PAGSTGQVVHGS PREGFWCLNREQ
RPGQNCNSNYTVRFLCPPGSLRRDTERIWS PWS PWSKCSAACGQTGVQTRTRICLAEVSLCS
EASEEGQHCMGQDCTACDLTCPMGQVNADC DACMCQDFMLHGAVSLPGGAPASGAAIYLLTK
TPKLLTQTDSDGRFRI PGLCPDGKSILKITKVKF APIVLTMPKTS LKAATIKA EFVRAETPY
MVMNPETKARRAGQSVSLCCKATGKPRPDKYFWYHNDTLLDPSLYKHE SKLVLRLQHQAG
EYFCKAQSDAGAVKS KVAQLIVTASDETPCNPVPESYLI RLPHDCFQNATNSFYYDVGRCPV
KTCAGQQDNGIRCRDAVQNCCGISKTEEREIQC SGYTLPTKVAKECSCQRCTETRSIVRGRV
SAADNGEPMRFGHV YMGN SRVSM TGKFTLHV P QDTERL VLT FVDR LQKFVNNTKVL PFN
KKGS AVFHEIKMLRRKEPITLEAMETNIIPLGEVVGEDPMAELEIPSRSFYRQN GEPYIGKV
KASVTFLDPRNISTATAAQTDLNFINDEGDTFPLRTYGMFSVDFRDEVTSEPLNAGKVKVHL
DSTQVKMPEHISTVKLWSLN PDTGLWEEEGDFKFENQRRNKREDRTFLVGNLEIRERRLFNL
DV PESRRCFVKVRAYR SERFLPSEQIQGVVISVINLEPRTGFLSNPRA WGRFDSVITGPNGA
CVPAFCDDQSPDAYSAYV LASLAGEELQAVESSPKFN PNAIGVPQPYLNKL NYRRTDHD EPR
VKKTAFQISMAKPRPNSAEE NGPIYAFENLRACEEAPP SAAHFRFYQIEGDRYDYNTVPFN
EDDPMSWTE DYLAWWP KPM EFRACYIKV KIVGPLEVNVR SRNMGGTH RRTVGKLYGIRD VRS
TRDRDQPNVSAACLEFKCSGMLYDQDRVDR TLV KVI PQGSCRRASVN PMLHEYLVNHLPLAV
NNDTSEYTM LAPLDPLGHNYGIYTVDQDPRTAKEIALGRCFDGTS DGSSRIMKS NVGVALT
FNCVERQVGRQSAFQYLQSTPAQSPAAGTVQGRVPSRRQQ RASRGGQRQGGVVASLRFPRVA
QQPLIN

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FIGURE 73

CTGCAAGTTGTTAACGCCAACACACAAGTATGTTAGGCTTCCACCAAGTCTCAATATACTGAATACGCAC
AATATCTTAACCTTCATATTGGTTGGGATCTGCTTGAGGCTCCATCTTCAATTAAAAAAATACAGAG
ACCTACCTACCCGTACGCATACATACATATGTATATATGTAAACTAGACAAAGATCGCAGATCATAAAGC
AAGCTCTGCTTAGTTCCAAGAAGATTACAAGAATTAGAGATGATTGTCAGATCCCTGTCGATTCTG
CCCTTGGGTTACGGTGTCTCAGTGATGCAGCCCTACCCCTGGTTGGGGACATTATGATTGTAAGACT
CAGATTACACGGAAGAAGGGAAAGTTGGGATTACATGGCTGCCAGCCGGAATCCACGGACATGACAAAATA
TCTGAAAGTGAAACTCGATCCTCCGGATATTACCTGTGGAGACCCCTCTGAGACGTTCTGTGCAATGGCAATC
CCTACATGTGCAATAATGAGTGTGATGCGAGTACCCCTGAGCTGGCACACCCCCCTGAGCTGATGTTGATT
GAAGGAAGACATCCCTCACATTGGCAGTCTGCCACTTGAAGGAGTATCCAAGCCTCTCAGGTTAACAT
CACTCTGTCTGGAGCAAACATTGAGCTAACAGACAACATAGTTAACCTTGAATCTGGCGTCCAGACC
AAATGATCCTGGAGAAGTCTCTGATTATGGACGAACATGGCAGCCCTATCAGTATTATGCCACAGACTGCTTA
GATGCTTTACATGGATCCTAACCTGGTGAAGGATTATCACGCTACGGCTTAACTGACAGAG
AGAGTACTCAACAGGGTATAACAAACATTGAAACAGGAAACTAACAGGTTGGCCTTTG
CTGGACCTCGCCTACGCAATATGGCTCCCTACGGACAGCTGGATACAAACAGGAAACTCAGAGATTCTT
ACAGTCACAGACCTGAGGATAAGGCTGTTAACGACAGCGTGGGAAATTGGTAGATGAGCTACACTTGGC
ACGCTACTTTACCGATCTCAGACATAAGGCTGAGGCTCCTATCTCCCCATCCCCAAAGGCACTGAAACACTGT
TGTATGACAACAGCAAATTGACATGCGAATGTGAGCACAACACTACAGGCTCAGACTGTGGGAAATGCAAGAAG
AATTATCAGGGCCGACCTGGAGTCCAGGCTCCTATCTCCCCATCCCCAAAGGCACTGAAACACTGT
CAGTATTCCAGTATTGGTACGAATGTCTGCGACAACGAGCTCCTGCACTGCCAGAACGGAGGGACGTGCCACA
ACAACGTGCGCTGCCGTGCCCGCATACACGGGCATCTCTGCGAGAACGCTGCCGTGCGAGGAGGCTGGC
AGCTGCGGCTCGACTTGGCAGGGCGGCCACGGCACCCAGCGCTGCTGCTGACCACGCTGCT
GGGAACCGCCAGCCCCCTGGTGTTC~~TAGGTGT~~CACCTCCAGGCCACACCAGCGACGGGCTGTGCCGTGGGAAGCA
GACACAACCCAAACATTGCTACTAACATAGGAAACACACATACAGACACCCCCACTCAGACAGTGTACAAA
CTAAGAAGGCCAACTGAACACTAACGCAATTATCACCGTGGACAGCACATCCGACTCAAGACTGTTAATTTC
TGACTCCAGAGGAGTTGGCAGCTGTTGATATTACTGCAAAATCACATGCCAGCTGCAAGACATATTGTGGA
TTGAAAGGCTGCGACAGCCCCAAACAGGAAAGACAAAAAAACAAACAAATCAACCGACCTAAACACATTGGC
TACTCTAGCGTGGTGCCTCTAGTACGACTCCGGCCAGTGTGTTGGACCAACCAAAATAGCATTCTTGT
GTGATTGTGGCATAAGGAAATCTGTTAACAGCTGCCATATTGGCTCTCCGTCCCTGAATCCCTTCAAC
CTGTGCTTAGTGAACGTTGCTGTAAACCTCGTGGTGAAGATTCTTGTCTGATGTTAGTGT
TGTAAACAGCCCCCTCTAAAGCGCAAGCCAGTCATACCCCTGTATATCTTAGCAGCACTGAGTCCAGTGC
GCACACACCCACTATACAAGAGTGGCTATAGGAAAAAGAAAGTGTATCTATCCTTTGTATTCAAATGAAGTT
ATTTTCTTGAACTACTGTAATATGTAGATTGGTATTATTGCCAATTGTGTTACAGACATCTGTTAAT
GTATCTAATTGCAATCAGCAAAGACTGACATTATTGTCTCTTCTGTTCTGTTGTTACTGTGCAGA
GATTCTCTGTAAGGGCAACGAACGCTGCTGGCATCAAAGAATATCAGTTACATATATAACAAGTGTAAATAAGA
TTCCACCAAAAGGACATTCTAAATGTTCTTGTGTTAACACTGGAAGATTAAAGAATAAAACTCCTGCA
TAAACGATTCAGGAATTGTATTGCAATTCTTAAGATGAAAGGAACAGCCACCAAGCAGTTACACT
TTACTGATTCTGTGTGGACTGAGTACATTCAAGCTGACGAATTAGTCCAGGAAGATGGATTGATGTTCACT
AGCTTGGACAACCTCTGCAAAATATGAGACTATTCCACTTGGAAAAATTACAACAGCAAAAAAA
AAAAAA

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FIGURE 74

MYLSRSLSIHALWTVSSVMQPYPLVGWGHYDLCKTQIYTEEGKVWDYMACQPESTDMTKYLK
VKLDPPDITCGDPPETFCAMGNPYMCNNEDASTPELAHPPELMFDFEGRHPSTFWQSATWK
EYPKPLQVNITLSWSKTIELTDNIVITFESGRPDQMILEKSLDYGRTWQPYQYYATDCLDAF
HMDPKSVKDLSQHTVLEIICTEEYSTGYTTNSKIIHFEIKDRFALFAGPRLRNMASLYGQLD
TTKKLRDFFTVDLIRIRLLRPAVGEIFVDELHLARYFYAISDIKVRGRCKCNLHATVCVYDN
SKLTCECEHNTTGPDCGKCKNYQGRPSPGSYLPPIPGBTANTCIPSISSIGTNVCDNELH
CQNGGTCHNNVRCLCPAAYTGILCEKLREEAGSCGSDSGQGAPPHTPALLLTTLLGTAS
PLVF

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FIGURE 75

CCACCGCGTCCGGGTGACCTGGGCCAGCCCTCCCGTCGGCTAAGATTGCTGAGGAGGCCG
CGGGTAGCTGGCAGGCAGCCGACTTCCGAAGGCCGCGTCCGGCGAGGGTGCCTCATGACTT
CTCTTGTGGACCATGTCCGTGATCTTTGCCTGCCTGGTACGGTAAGGGATGGACTGCC
CCTCTCAGCCTCTACTGATTTTACACACCCAAGATTTTGGAAATGGAGGAGACGGCTCA
AGAGTTAGCCTTGCAGTGGCCAGTATCCAGGTGAGGTTCTGCAGAAGGTTGTGACTTT
AGTATACATTTTCTTCTTCCGGGACGTGGCCTGCATGGCTATCTGCTCCTGCCAGTGTCC
AGCAGCCATGGCCTCTGCTTCCGGAGACCCCTGTGGTGGAAATTACAGCTTCCATGACA
CTACCTGCATTGGCCTAGCCTCCAGGCCATACGCTTTCTTGAGTTGACAGCATTCA
AAAGTGAAGTGGCATTAACTATGTAAGTTCCTCTCAGATGGAGTGCAGCTTGGAAAAAAT
TCAGGAGGAGCTCAAGTTGCAGCCTCCAGCGTTCTCACTCTGGAGGACACAGATGTGGCAA
ATGGGGTGTGAATGGTCACACACCGATGCAGTGGAGCCTGCTCTAATTCGAATGGAA
CCAGTGACAGCCCTGGGTATCCTCTCCCTCATTCTAACATCATGTGTGCTGCCCTGAATCT
CATTCGAGGAGTTCACCTGCAGAACATTCTTACAGGATCCAAGGAGCTGGTCTGCTGGT
TGGACCAAACCTCGTGAGCCAGCCACCCCTGACCCAAATGAGGAGAGCTCTGATTCTCCCAT
CCGGGAGCAGTGTCAAACCTCTGCTGCTGGGAAATCTCATCAGCAGGGAGCCTGTGGA
AAAGGGCATGTCAGTGAATCTGGGAATGGCTGGATTGGAAACATCTGCCATGTGTATTG
ATGGCAGAGCTGTTGCCCAAGCGCCTTTATTAGGGTAAAATTAACAAATCCATTCTAT
TCCTCTGACCCATGCTTAGTACATATGACCTTAACCCCTACATTATGATTCTGGGGTT
GCTTCAGAAGTGTATTGATCATGATTCATATGATTGATCCCCCAGGATTCTATTTGT
TTAATGGGCTTTCTACTAAAAGCATAAAATCTGAGGCTGATTAGTCAGGGCAAAACCAT
TTACTTTACATATTGTTCAATACTTGCTGTTCATGTTACACAAGCTTACGGTTTC
TTGTAACAATAAAATTTGAGTAAATAATGGGTACATTTAACAAACTCAGTAGTACAACC
TAAACTGTATAAAAGTGTGAAAATGTATAGCCATTATATCCTATGTATAAATTAAATG
AGGTGGCTTCAGAAATGGCAGAATAAATCTAAAGTGTATTAAAAA
AAAAG

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FIGURE 76

MSVIFFACVVVRVRDGLPLSASTDFYHTQDFLEWRRRLKSLALRLAQYPGRGSAEGCDFSIHF
SSFGDVACMAICSCQCPAAMAFCFLETLWWFTASYDTTCIGLASRPYAFLEFDSIIQKVKW
HFNYVSSSQMECSLEKIQEELKLQPPAVLTLEDTDVANGVMNGHTPMHLEPAPNFRMEPVTA
LGILSLILNIMCAALNLIRGVHLAEHSLQDPRSWFCWLDQTS

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FIGURE 77

TGCTTCCTGGAGACCCGTGGTGGGAATCACAGCTCNTATGACACTACCTGCATTGGCNT
AGCCTCCAGGCCATACGCTTTCTTGAGTTGACAGCATTCAGAAAGTGAAGTGGCATT
TTAACTATGTAAGTTCTNTCAGATGGAGTGCAGCTTGGAAAAAATTCAAGGAGGAGCTCAAG
TTGCAGCCTCCAGCGGTTCTCANTATGGAGGACACAGATGTGGCAAATGGGT

FIGURE 78

CTCAGCGGGCGTTCTCGTAGCGAGCCTAGTGGCGGGTGTTCGATTGAAACGTGAGCGCGA
CCCGACCTTAAAGAGTGGGGAGCAAAGGGAGGACAGAGCCCTTAAACAGAGGCGGGTGGTG
CCTGCCCTTAAGGGCGGGCGTCCGGACACTGTATCTGAGCCCCAGACTGCCCGAGTT
TCTGTCGAGGCTGCGAGGAAAGGCCCTAGGCTGGTCTGGGTCTGGCAGGGCGGCTT
CCTCCCCGCTCGTCCCTCCCCGGGCCAGAGGCACCTCGGCTCAGTCATGCTGAGCAGAGTA
TGGAAGCACCTGACTACGAAGTGTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGC
GAGTGTATTATATCAACACTCTGTTGCAACACTGTACATCCTGCCACATCTTCCTGAC
CCGCTTCAAGAACGCTGCTGAGTTACACACAGTGGATGATGAAGATGCCACCGTCAACAAGA
TTGCGCTCGAGCTGTCACCTTACCCCTGGCAATTGCCCTGGTCTGCTCTGCC
TTCTCCATCATCAGCAATGAGGTGCTGCTCCCTGCCCTCGGAACCTGTTTCTTCCCTCA
CAACGGCTCCCTCATCCATGCCCTCGGAACCTGTTTCTTCCCTCA
TCTCCTCATGCCCTTGCAATTCTACTGAGTCTGAGGGCTTGCTGGCTCCAGAAAG
GGTGCCTGGGCCGGTCTATGAGACAGTGGTGTGATGCTCCTCACTCTGCTGGTGT
AGGTATGGTGTGGGTGGCATCAGCATTGTTGACAAGAACAGGCAACAGAGAGTCACCT
ATGACTTTGGGAGTACTATCTCCCTACCTCTACTCATGCATCTCCTCTGGGTTCTG
CTGCTCCTGGTGTACTCCACTGGGTCTGCCCGCATGTTCTCCGTACTGGGAAGCTGCT
AGTCAAGCCCCGGCTGCGAACGACCTGGAGGAGCAGCTGACTGCTCAGCCTTGAGGAGG
CAGCCCTGACCCGCAGGATCTGTAATCCTACTTCCCTGCTGGCTGCCCTTAGACATGGAGCTG
CTACACAGACAGGTCTGGCTCGCAGACACAGAGGGCTGCTGGAGAACAGGGCGGAAGGC
TTCAGCCTGCAACGGAACCTGGCTACCCCTGGCTATGCTGCTGCTGGTGTGACGG
GCCTGTCTGTGCTCATTGTGGCCATCCACATCCTGGAGCTGCTCATCGATGAGGCTGCCATG
CCCCGAGGCATGCAGGGTACCTCCTAGGCCAGGTCTCCTCTCCAAGCTGGCTCC
TGCCGTATTCAAGGTTGACTCATCTTACCTAATGGTGTCTCAGTTGTGGCTTCTATA
GCTCTCCACTCTCCGGAGCCTGCGGCCAGATGGCACGACACTGCCATGACGCA
GGAACTGTGTCTGTCCTGGCCTAACGCTCAGCACTCCCTGCTTCTCTCGAACCTGG
GCTCACTCGCTTGACCTGCTGGGTGACTTTGGACGCTCAACTGGCTGGCAATTCTACA
TTGTGTTCTCTACACGCAAGCTTGGCAGGCTCACCACACTCTGCTGGTGAAGACCTC
ACTGCAGCTGTGCGGGCAGAGCTGATCCGGCCTTGGCTGGACAGACTGCCGTGCC
CTCCGGTTCCCCCAGGCATCTAGGAAGACCCAGCACCAG**TGA**CTCCAGCTGGGGTGG
AGGAAAAAAACTGGACACTGCCATCTGCTGCCAGGGCTGGAGGGAGCAGGCCATCTGCA
ACCTCAGGACCTGGAATCTGAGAGGGTGGCTGGCAGAGGGAGCAGGCCATCTGCA
GCATAATCTGAGCCAGAGTTGGGACCAAGGACCTCCTGCTTTCCATACTTA
CAGCATGGGGTAGGGCTGGGTGACTGGGTCTAGCCCTGATCCAAATCTGTTACACATCA
ATCTGCCACTGCTGTTCTGGCCATCCCCATGCCATGTTACATGATTGATGTGCA
AGGGTGGGGTAGGGCAGGGAAAGGACTGGGCAGGGCAGGCTGGAGGATAGATTGTCTCC
CTTGCTCTGGCCCAGCAGAGCTAACGACTGTGCTATCTGGAGGGCTTGAC
AAAGACCAAGGGATAGGGAGGAGGAGGCTCAGCCATCAGCAATAAGTTGATCCCAGGG
AAAAAA

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FIGURE 79

MEAPDYEVLSVREQLFHERIRECIISTLLFATLYILCHIFLTRFKKPAEFTTVDDEDATVNK
IALELCTFTLAIALGAVLLLPSIISNEVLLSLPRNYYIQWLNGSLIHGLWNLVFLFPNLSL
IFLMPFAYFFTESEGFAGSRKGVLGRVYETVVMLMLTLLVLGMVWVASAIVDKNKANRESL
YDFWEYYLPYLYSCISFLGVLLLLVCTPLGLARMFSVTGKLLVKPRLLEDLEEQLYCSAFEE
AALTRRICNPTSCWLPLDMELLHRQVLALQTQRVILLEKRRKASAWQRNLGYPLAMLCLLVLT
GLSVLIVAIHILELLIDEAAMPQGMQGTSLGQVSFSKLGSGAVIQVVLIFYLMVSSVVGFY
SSPLFRSLRPRWHTAMTQIIGNCVCLVLSSALPVFSRTLGLTRFDLLGDFGRFNWLGNFY
IVFLYNAAFAGLTTLCLVKTFTAAVRAELIRAFGLDRLPLPVSGFPQASRKTQHQ

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FIGURE 80

GGCTGCCGAGGGAAAGGCCCTGGGTTGGTCTTGGTTGCTTGGCGGCGGNTCNTCCCC
GCTCGTCCTCCCCGGGCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGAAGC
ACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCCGAGTGTA
TTATATCAACACTTCTGTTGCAACACTGTACATCCTCTGCCACATCTCCTGACCCGCTTC
AAGAAGCCTGCTGAGTTACCCACAGTGGATGATGAAGATGCCACCG

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FIGURE 81

GACCGACCTTAAAGAGTGGGAGCAAAGGGAGGACAGAGCCTTTAAAACGAGGCAGGTGGTGC
CTGCCCTTAAGGGCGGGCGTCCGGACACTGTATCTGAGCCCCAGACTGCCCGAGTTTC
TGTGCAGGCTGCGAGGAAAGGCCCTAGGCTGGTCTGGTCTGGCGGCGGCGGCTTCCT
CCCCGTTGTCNTCCCCGGGCCAGAGGCACCTCGGCTTCAGTCATGCTGAGCAGAGTATGGA
AGCACCTGACTACGAAGTGCTATCCGTGCGAGAACAGCTATTCCACGAGAGGATCCGCGAGT
GTATTATATCAACACTTCTGTTGCAACACTGTACATCNTCTGCCACATTTCCCTGACCCGC
TTCAAGAAGCCTGCTGAGTCACCACAGTGGATGATGAAGATGCCACCGTCAACAAGATTGC
GCTCGAGCTGTGCACCTTACCTGGCAATTGCCCTGGTGCCTGCTCCTGCCCTTCT
CCATCATCAGCAATGAGGTGCTGCACTCCC

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FIGURE 82

GATGTGCTCCTGGAGCTGGTGTGCAGTGCCTGACTGTAAGATCAAGTCCAAACCTGTTT
GGAATTGAGGAAACTTCTCTTTGATCTCAGCCCTGGTGGCCAGGTCTCATGCTGCTGT
GGGTGATATTACTGGTCCTGGCCTGTCAGTGGACAGTTGCAAGGACACCCAGGCCATT
ATTTCTCCAGCCTCCATGGACCACAGTCTCCAAGGAGAGAGTGCACCTCACTTGCAA
GGGATTCGCTTCTACTCACCACAGAAAACAAATGGTACCATCGGTACCTGGAAAGAAA
TACTAAGAGAAACCCAGACAAATCCTTGAGGTCAGGAATCTGGAGAGTACAGATGCCAG
GCCAGGGCTCCCTCTCAGTAGCCCTGTGCACTGGATTTCTCAGAGATGGGATTCC
TCATGCTGCCAGGCTAATGTTGAACTCCTGGCTCAAGTGTCTGCTCACTAGGCCTCTC
AAAGCGCTGGGATTACAGCTTCGCTGATCCTGCAAGCTCCACTTCTGTGTTGAAGGAGAC
TCTGTGGTTCTGAGGTGCCGGCAAAGGCGGAAGTAACACTGAATAACTATTACAAGAA
TGATAATGTCCTGGCATTCTTAATAAAAGAACTGACTTCCAAAAAAA
AAA

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FIGURE 83

MLLWVILLVLA
PVSGQFARTPRPIIFLQPPWTTVFQGERVLTCKGFRFYSPQKTKWYHRYL
GKEILRETPDNILEVQESGEYRCQAQGSPPLSSPVHDFSSEMGFPHAAQANVELLGSSDLLT

FIGURE 84

CAGAAGAGGGGGCTAGCTAGCTGTCTCGGGACCAGGGAGACCCCCCGCGCCCCCGGTGT
GAGGCGGCCCTCACAGGGCCGGGTGGCTGGCGAGCCGACGCCGGCGGAGGAGGCTGTGAG
GAGTGTGTGGAACAGGACCCGGACAGAGGAACC**ATG**GCTCCGCAGAACCTGAGGACACCTTT
GCCTGTTGCTGCTATACTCATCGGGCGGTGATTGCCGGACGAGATTCTATAAGATCTG
GGGGTGCCTCGAAGTGCCTCTATAAAGGATATTAAAAAGGCCTATAGGAAACTAGCCCTGCA
GCTTCATCCGACCAGAACCCCTGATGATCCACAAGCCCAGGAGAAATTCCAGGATCTGGGTG
CTGCTTATGAGGTTCTGTCAGATAGTGAGAAACGGAAACAGTACGATACTTATGGTGAAGAA
GGATTAAAAGATGGTCATCAGAGCTCCCATGGAGACATTTTCACACTCTTGGGGATT
TGGTTTCATGTTGGAGGAACCCCTCGTCAGCAAGACAGAAATATTCCAAGAGGAAGTGATA
TTATTGTAGATCTAGAAGTCACTTGGAAGAAGTATATGCAGGAAATTGTGGAAGTAGTT
AGAAAACAAACCTGTGGCAAGGCAGGCTCTGGCAAACGGAAGTGCAATTGTCGGCAAGAGAT
GCGGACCACCCAGCTGGCCCTGGCGCTTCAAATGACCCAGGAGGTGGTCTGCGACGAAT
GCCCTAATGTCAAACACTAGTGAATGAAGAACGAACGCTGGAAAGTAGAAATAGAGCCTGGGGTG
AGAGACGGCATGGAGTACCCCTTATTGGAGAAGGTGAGCCTCACGTGGATGGGGAGCCTGG
AGATTTACGGTTCCGAATCAAAGTTGTCAAGCACCCAAATATTGAAAGGAGAGGAGATGATT
TGTACACAAATGTGACAATCTCATTAGTGAGTCACTGGTTGGCTTGAGATGGATATTACT
CACTTGGATGGTCACAAGGTACATATTCCCGGGATAAGATCACCAGGCCAGGAGCGAAGCT
ATGGAAGAAAGGGGAAGGGCTCCCAACTTGACAACAACAATATCAAGGGCTTTGATAA
TCACTTTGATGTGGATTTCCAAAAGAACAGTTAACAGAGGAAGCGAGAGAAGGTATCAA
CAGCTACTGAAACAAGGGTCAGTGCAGAAGGTACAAATGGACTGCAAGGATAT**TGA**GAGTG
AATAAAATTGGACTTGTAAAATAAGTAATAAGCGATATTATTATCTGCAAGGTTTT
TTGTGTGTGTTTGTGTTATTCAATATGCAAGTTAGGCTTAATTTTTATCTAATGA
TCATCATGAAATGAATAAGAGGGCTTAAGAATTGTCCATTGCATTGGAAAAGAATGACC
AGCAAAAGGTTACTAATACCTCTCCCTTGGGATTTAATGTCTGGTGTGCCGCTGAGT
TTCAAGAATTAAAGCTGCAAGAGGACTCCAGGAGCAAAAGAAACACAATATAGAGGGTTGGA
GTTGTTAGCAATTCAAAATGCCAACTGGAGAAGTCTGTTTAAATACATTGTTG
TTATTTTA

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FIGURE 85

MAPQNLSTFC~~LLL~~YLIGAVIAGRDFYKILGVPRSASIKDIKKAYRK~~L~~ALQLHPDRNPDDPQ
AQEKFQDLGAAYEVLS~~D~~SEKRQYDTYGE~~E~~GLKDGHQSSHG~~D~~IFSHFFGDFGMFGGT~~P~~RQQ
DRNIPRGSDII~~V~~LEV~~T~~LEE~~V~~YAGNF~~V~~EV~~V~~R~~N~~K~~P~~VARQ~~A~~P~~G~~K~~R~~K~~C~~N~~R~~Q~~E~~M~~R~~TTQLG~~P~~GRFQ
MTQE~~V~~VC~~E~~CPNV~~K~~L~~V~~NEERT~~L~~EV~~E~~IEPG~~V~~R~~D~~G~~M~~E~~Y~~P~~F~~IGE~~G~~E~~H~~V~~D~~G~~E~~P~~G~~D~~L~~R~~F~~R~~I~~K~~V~~V~~K~~
PIFERRGDDLYTNVTISL~~V~~E~~S~~L~~V~~G~~F~~EM~~D~~IT~~H~~LDGH~~K~~V~~H~~I~~S~~R~~D~~K~~I~~T~~R~~P~~G~~A~~K~~L~~W~~K~~K~~G~~E~~GL~~P~~N~~F~~
NNNIKGSLI~~I~~ITFDVDFP~~K~~EQ~~L~~TE~~E~~AREGI~~K~~Q~~L~~L~~K~~Q~~G~~S~~V~~Q~~K~~V~~Y~~N~~G~~Q~~G~~Y

Important features:**Signal peptide:**

amino acids 1-22

Cell attachment sequence.

amino acids 254-257

Nt-dnaJ domain signature.

amino acids 67-87

Homologous region to Nt-dnaJ domain proteins.

amino acids 26-58

N-glycosylation site.

amino acids 5-9, 261-265

Tyrosine kinase phosphorylation site.

amino acids 253-260

N-myristoylation site.

amino acids 18-24, 31-37, 93-99, 215-221

Amidation site.

amino acids 164-168

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FIGURE 86

TGGGACCAGGGAACCCGGGCCCCCGGTGGAGNGCTAACAGGCCGGTGGNTGCGACCGAA
GCGGCGGGCGGAGGAGGTTTGAGGATTTGGAACAGGACCCGGACAGAGGAACCATGGTT
CCGCAGAACNTGAGCACNTTGCCTGTTGNTGNTATACTTCATCGGGCGGTGATTGCCGG
ACGAGATTTNTATAAGATTTGGGTGCCTNGAAGTGCCTNTATAAAGGATATTAAAAAGG
CCTATAGGAAACTAGCCCTGCAGNTTATCCCGACCGGAACCCCTGATGATCCACAAGCCCAG
GAGAAATTCCAGGATTGGGTGCTGCTTATGAGGTTNTGTCAGATAGTGAGAACGGAAACA
GTACGATAATTATGGTGAAGAAGGATTAAGATGGTNATCAGAGCTCCATGGAGACATT
TTTCACACTNTTGGGATTTGGTTCATGTTGGAGGAACCCCTNGTCAGCAAGACAGA
AATATTCCAAGAG

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FIGURE 87

GGCACGAGGCAGGGGGCAGTCGCGGGATGCGCCCGGGAGCCACAGCCTGAGGCCCTCAGGT
CTCTGCAGGTGTCGTGGAGGAACCTAGCACCTGCCATCCTCTCCCCAATTGCCACTCCA
GCAGCTTAGGCCATGAGGAGGATGTGACCGGGACTGAGTCAGGAGCCCTCTGGAAGC**ATGG**
AGACTGTGGTATTGTTGCCATAGGTGTGCTGCCACCACATCTTCTGGCTTCGTTGCAGCC
TTGGTGCTGGTTGCAGGCAGCGCTACTGCCGGCCCGAGACCTGCTGCAGCGCTATGATT
TAAGCCCATTGTGGACCTCATTGGGCCATGGAGACCCAGTCTGAGCCCTCTGAGTTAGAAC
TGGACGATGTCGTTATCACCAACCCCCACATTGAGGCCATTCTGGAGAATGAAGACTGGATC
GAAGATGCCTCGGGTCTCATGTCCCAGTCATTGCCATCTGAAGATTGTCACACTCTGAC
AGAGAAGCTGTTGCCATGACAATGGGCTCTGGGCCAAGATGAAGACTTCAGCCAGTGTCA
GCGACATCATTGTGGTGGCCAAGCGGATCAGCCCCAGGGTGGATGATGTTGTGAAGTCGATG
TACCCCTCCGTTGGACCCAAACTCCTGGACGCACGGACGACTGCCCTGCTCCTGTCTGCA
TCACCTGGTGTGGTACAAGGAATGCCATCTGACGGGAGGCCTGGACTGGATTGACC
AGTCTCTGTCGGCTGCTGAGGAGCATTGGAAGTCCTCGAGAAGCAGCCCTAGCTTCTGAG
CCAGATAAAGGCCTCCCAGGCCCTGAAGGGCTCTGCAGGAGCAGTCTGCAATT**TAGTGCCT**
ACAGGCCAGCAGCTAGCCATGAAGGCCCTGCCGCATCCCTGGATGGCTCAGCTTAGCCTT
CTACTTTTCTATAGAGTTAGTTGTTCTCCACGGCTGGAGAGTTCAAGCTGTGTGCATAG
TAAAGCAGGAGATCCCCGTCAAGTTATGCCCTTTGCAAGTGCACACTGTGGCTGGTGA
GGCAGTCTAATACTACAGTTAGGGAGATGCCATTCACTCTGCAAGAGGAGTATTGAAA
CTGGTGGACTGTCAGCTTATTAGCTCACCTAGTGTTCAGCAAGAAAATTGAGGCCACCGTCT
AAGAAAATCAAGAGGTTTCACATTAAAATTAGAATTCTGGCCTCTCGATCGGTAGAATG
TGTGGCAATTCTGATCTGCATTTCAGAAGAGGACAATCAATTGAAACTAAGTAGGGGTTTC
TTCTTTGGCAAGACTTGTACTCTCTCACCTGGCCTGTTCAAGTATTGTATTATCTGCCT
GGTCCCTGAGGCGTCTGGGTCTCCCTCCCTGGCAGGTTGGGTTGAAGCTGAGGAAC
ACAAAGTTGATGATTCTTTTATCTTATGCCCTGCAATTACCTAGCTACCACTAGGTG
GATAGTAAATTATACTTATGTTCCCTCAAAAAAAAAAAAAAA

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FIGURE 88

METVVIVAI^GVLATI^FLASFAALVLVCRQRYCRPRD^LLQRYDSKPIV^DLIGAMETQSEPSEL
ELDDVVITNPHIEAILENEDWIEDASGLMSHCIAILKICHTL^TEKL^VAMTMGSGAKMKT^SAS
VSDIIVVAKRISPRVDDVVKS^MY^PPLDPKLLDARTTALLSVSHLV^LVTRNACHLTGGLDW^I
DQSLSAAEEHLEVLREAALASEPD^KGLPGPEGFLQE^QSAI

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FIGURE 89

GCTTCATTCCTCCCGACTCAGCTTCCCACCCCTGGGCTTCCGAGGTGCTTCGCCGCTGTCC
CCACCACTGCAGCCATGATCTCCTTAACGGACACGCAGAAAATTGAATGGGATTAACAGGA
TTTGGAGTGTTCCTGTTCTGGAAATGATTCTCTTTGACAAAGCACTACTGGCTAT
TGGAAATGTTTATTGTAGCCGGCTTGGCTTTGTAATTGGTTAGAAAGAACATTCAAGAT
TCTTCTCCAAAAACATAAAATGAAAGCTACAGGTTTTCTGGGTGGTATTGTAGTC
CTTATTGGTGGCCTTGATAGGCATGATCTCGAAATTATGGATTTCTCTGTCAG
GGGCTTCTTCCTGTCGTTGGCTTATTAGAAGAGTGCCAGTCCTGGATCCCTCCTAAAT
TTACCTGGAATTAGATCATTGTAGATAAAAGTTGGAGAAAGCAACAATATGGTATAAACA
AGTGAATTGAAGACTCATTAAAATATTGTGTTATTATAAAAGTCATTGAAGAATATTCA
GCACAAAATTAAATTACATGAAATAGCTTGTAAATGTTCTTACAGGAGTTAAACGTATAG
CCTACAAAGTACCAAGCAGCAAATTAGCAAAGAAGCAGTGAAACAGGCTTCAACTCAAGTGA
ACTAAGAAGAAGTCAGCAAGCAAATGAGAGAGGTGAAATCCATGTTAATGATGCTTAAGAA
ACTCTTGAAGGCTATTGTGTTGGCTTCCACAATGTGCGAAACTCAGCCATCCTTAGAGAA
CTGTGGTGCCTGTTCTTTCTTTATTGAAAGGCTCAGGAGCATCCATAGGCATTGCT
TTTAGAAGTGTCCACTGCAATGGAAAAATATTCCAGTTGCACTGTATCTCTGGAAGTGA
TGCATGAATTGATTGGATTGTGTCATTAAAGTATTAAAACCAAGGAAACCCCAATTG
ATGTATGGATTACTTTTTGNGNCAGGGCC

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FIGURE 90

MISLTDTQKIGMGLTGFVFFLFFGMILFFDKALLAIGNVLFVAGLA
FVIGLERTFRFFFQK
HKMKATGFFLGGVFVVLIGWPLIGMIFEIYGFFLLFRGFFPVVVG
FIRRVPVLSLLNLPGI
RSFVDKVGESNNMV

Important features:

Transmembrane domains:

amino acids 12-30 (typeII), 33-52, 69-89 and 93-109

N-myristoylation sites.

amino acids 11-16, 51-56 and 116-121

Aminoacyl-transfer RNA synthetases class-II protein.

amino acids 49-59

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FIGURE 91

GAAGACGTGGCGGCTCTGCCTGGCTGTTCCCGGCTTCATTCCTCCGACTCAGCTTCCC
ACCNTGGGCTTCCGAGGTGCTTCGCCGCTGTCCCCACCACTGCAGCCATGATCTCCTTAA
CGGACACGCAGAAAATTGGAATGGGATTAACCGGATTGGAGTGTTTCCTGTTCTTGGAA
ATGATTCTCTTTTGACAAAGCACTACTGGCTATTGGAAATGTTTATTGTAGCCGGCTT
GGCTTTGTAATTGGTTAGAAAGAACATTAGATTCTTCCAAAAACATAAAATGAAAG
CTACAGGTTTTCTGGGTGGTATTGTAGTCCTATTGGTTGGCCTTGATAGGCATG
ATCTCGAAATTTATGGATTTCTCTGTTC

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FIGURE 92

GGCACGAGGCTGAACCCAGCCGGCTCCATCTCAGCTCTGGTTCTAAGTCCATGTGCCAAA
GGCTGCCAGGAAGGAGACGCCTCCTGAGTCCTGGATCTTCTTCCTCTGGAAATCTTGA
CTGTGGGTAGTTATTCTGAATAAGAGCGTCCACGCATCATGGACCTCGCGGGACTGC
TGAAGTCTCAGTTCTGTGCCACCTGGTCTCTGCTACGTCTTATTGCCTCAGGGCTAATC
ATCAACACCATTAGCTCTTCACTCTCCCTCTGGCCCATTAACAAGCAGCTCTCCGGAA
GATCAACTGCAGACTGTCCTATTGCATCTCAAGCCAGCTGGTGTGCTGGAGTGGTGGT
CGGGCACGGAATGCACCATCTCACGGACCCGCGCGCTACCTCAAGTATGGGAAGGAAAAT
GCCATCGTGGTCTCAACCACAAGTTGAAATTGACTTCTGTGTGGCTGGAGCCTGTCCGA
ACGCTTGGGCTTGTAGGGGCTCCAAGGTCTGGCCAAGAAAGAGCTGGCCTATGTCCCAA
TTATCGGCTGGATGTGGTACTTCACCGAGATGGTCTTCTGTCGCGCAAGTGGGAGCAGGAT
CGCAAGACGGTTGCCACCAAGTTGCAGCACCTCCGGGACTACCCCGAGAAGTATTTTCCCT
GATTCACTGTGAGGGCACACGGTTCACGGAGAAGAACATGAGATCAGCATGCAGGTGGCCC
GGGCCAAGGGGCTGCCCTGCCCTCAAGCATTGTCACCGAACCAAGGGCTTCGCCATC
ACCGTGAGGAGCTTGAGAAATGTAGTTCAGCTGTATATGACTGTACACTCAATTTCAGAAA
TAATGAAAATCCAACACTGCTGGAGTCCTAACGGAAAGAAATACCATGCAGATTTGTATG
TTAGGAGGATCCCCTGGAAGACATCCCTGAAGACGATGACGAGTGCTCGGCCTGGCTGCAC
AAGCTCTACCAAGGAGAAGGATGCCCTTCAGGAGGAGTACTACAGGACGGGCACCTTCCCAGA
GACGCCATGGTGCCCTGGGCCCTGGACCCCTCGTAAGTGGCTGGCTGGCCTCG
TGGTGTCTACCCCTTCTTCAGTTCTGGTCAGCATGATCAGGAGCGGTCTTCCCTGACG
CTGGCCAGCTTCATCCTCGTCTTGTGGCTCCGTGGAGTCATGGATGATTGGTGT
GACGGAAATTGACAAGGGCTTCAGGCAACTCTGACAGCAAGCAGAAACTGAATGACT**G**
ACTCAGGGAGGTGTACCATCCGAAGGGAACCTGGGAACGGCTCTGCATATCCT
CCTTAGTGGGACACGGTGACAAAGGCTGGGTGAGCCCTGCTGGGCACGGCGGAAGTCACGA
CCTCTCCAGCCAGGGAGTCTGGCTCAAGGCCGGATGGGAGGAAGATGTTTGTAAATCTT
TTTCCCCATGTGCTTAGTGGCTTGGTTGGTTGTGCGAGTGTGTGAGAATGGC
TGTGTGGTGAGTGTGAACCTTGTGATCATAGAAAGGGTATTTAGGCTGCAGGGAG
GGCAGGGCTGGGACCGAAGGGACAAGTCCCTTCATCCTTGGTGCTGAGTTCTGT
AACCTGGTGCAGAGATAAGTAAAAGTGTAGGTGAGATGACTAAATTATGCC
CAAGAAAAAAAAAAATAAAGTGTCTGGTCAAAAAAAAAAA

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FIGURE 93

MDLAGLLKSQFLCHLVFCYVFIASGLIINTIQLFTLLLWPINKQLFRKINCRLSYCISSQLV
MLLEWWSGTECTIFTDPRAYLKYGKENAIVVLNHKFEIDFLCGWSLSERFGLLGGSKVLAKK
ELAYVPIIGWMWYFTEMVFCSRKEQDRKTVATSLQHLRDYPEKYFFLIHCEGTRFTEKKHE
ISMQVARAKGLPRLKHHLLPRTKGFAITVRSLRNVVSAVYDCTLNFRNNENPTLLGVNLNGKK
YHADLYVRRIPLEDIPEDDDECASWLHKLYQEKDFAQEEYYRTGTFPETPMVPPRRPWTLVN
WLFWASLVLYPFFQFLVSMIRSGSSLTLASFILVFFVASVGVRWMIGVTEIDKGSAVGNSDS
KQKLND

FIGURE 94

CTGAGGCAGCGGTAGCATGGAGGGGGAGAGTACGTCGGCGGTGCTCTCGGGCTTGTGCTCG
GCGCACTCGCTTCCAGCACCTAACACGGACTCGGACACGGAAGGTTTCTTCTGGGAA
GTAAAAGGTGAAGCCAAGAACAGCATTACTGATTCCAAATGGATGATGTTGAAGTTGTTA
TACAATTGACATTGAGAAATATATTCCATGCTATCAGCTTTAGCTTTATAATTCTCAG
GCGAAGTAAATGAGCAAGCACTGAAGAAAATATTCAAATGTCAAAAGAATGTGGTAGGT
TGGTACAAATTCCGTCGTCAATTGAGATCATGACGTTAGAGAGAGGCTGCTTCACAA
AAACTTGAGGAGCATTTCAAACCAAGACCTGTTCTGCTATTAACACCAAGTATAA
TAACAGAAAGCTGCTACTCATGACTGGAACATTCTTATATAAACCTCAAAAGGACTT
TTTCACAGGGTACCTTAGTGGTGCCTGCAACTGGGCATGTCGAACAACGTGGTTATAAAC
TGTATCAGGTTCTGTATGTCCACTGGTTAGCCGAGCAGTACAAACACAGCTCTAAAT
TTTTGAAGAAGATGGATCCTTAAAGGAGGTACATAAGATAATGAAATGTATGCTTCATTA
CAAGAGGAATTAAAGAGTATATGCAAAAAAGTGGAAAGACAGTGAACAAGCAGTAGATAAACT
AGTAAAGGATGTAACAGATTAAACGAGAAATTGAGAAAAGGAGAGGAGCACAGATTCAAGG
CAGCAAGAGAGAAGAACATCCAAAAGACCTCAGGAGAACATTCTTGTCAAGGCATTA
CGGACCTTTTCAAATTCTGAATTCTCATTGATGTGTATGTCTTAAAAATAGACA
TGTTCTAAAGTAGCTGTAACATACAACCACATCTGATGTAGTAGACAATCTGACCTTAA
TGGTAGAACACACTGACATTCTGAAGCTAGTCCAGCTAGTACACCACAAATCATTAAGCATT
AAAGCCTTAGACTTAGATGACAGATGGCAATTCAAGAGATCTGGTTGTAGATACACAAGA
CAAACGATCTAAAGCAAATCTGGTAGTAGTAACCAAGATAAGCATCCAAAATGAGCAGCC
CAGAAACAGATGAAGAAATTGAAAAGATGAAGGGTTGGTGAATATTCAAGGCTCCTACA
TTTGATCCCTTTAACCTTACAAGGAGTTTTTATTGGCTGATGGTAAAGCCAAACAT
TTCTATTGTTTACTATGTTGAGCTACTGCACTAAGTCATTGTTACTATGTTCAC
CTGTTGCACTAATACACAGATAACTCTTAGTGCATTACTCACAAAGTACTTTCAAAC
ATCAGATGCTTTATTCCAAACCTTTTACCTTCACTAAGTTGAGGGGAAGGCT
TACACAGACACATTCTTAGAATTGAAAAGTGAAGGACAGGACAGTGGCTCACACCTGAA
TCCCAGCACTAGGGAAGACAAGTCAGGAGGATTGATTGAAGCTAGGAGTTAGAGACCAGCC
TGGGCAACGTATTGAGACCATGTCTATTAAAAAATAAAATGGAAAAGCAAGAATAGCCTTAT
TTCAAAATATGGAAAGAAATTATGAAAATTATCTGAGTCATTAAATTCTCCTTAAG
TGATACTTTTAAAGTACATTGGCTAGAGTTGCCAGATAAAATGCTGGATATCATGCA
ATAAAATTGCAAAACATCATCTAAATTAAAAAAAAAAAAAA

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FIGURE 95

MEGESTSAVLSGFVLGALAFQHLNTDSDEGFLLGEVKGEAKNSITDSQMDDVEVVYTIDIQ
KYIPCYQLFSFYNSGEVNEQALKKILSNVKKNVVGWYKFRRHSDQIMTFRERLLHKNLQEH
FSNQDLVFLLLTPSIITESCSTHRLEHSLYKPQKGLFHRVPLVVANLGMSEQLGYKTVSGSC
MSTGFSRAVQTHSSKFFED GSLKEVHKINEMYASLQEELKSICKVEDSEQAVDKLVKDVN
RLKREIEKRRGAQIQAAREKNIQKDPQENIFLCQALRTFFPNSEFLHSCVMSLKNRHVKSS
CNYNHLDVVDNLTLMVEHTDIP EASPASTPQIIKHKALD LDDRWQFKRSRLLDTQDKRSKA
NTGSSNQDKASKMSSPETDEEIEKMKGFG EYSRSPTF

FIGURE 96

GGCACAGCCGCGCGGGAGGGCAGAGTCAGCCGAGCCGAGTCCAGCCGGACGAGCGGACCAGCGCAGGGCAGC
CCAAGCAGCGCGCAGCGAACGCCGCCGCCACACCCCTCTGGTCCCCCGCGCCTGCCACCCCTCC
CCTCCCCCGCGTCCCCGCCCTGCCGGCCAGTCAGCTTGCCGGGTCGCTGCCCGCGAAACCCCGAGGTACCA
GCCCGCGCCTCTGCTTCCCTGGGCCGCGCGCCCTCCACGCCCTCTTCTCCCTGGCCCGGCCCTGGCACC
GGGGACCGTTGCGCTGACCGGAGGCCAGCTCTACTTTGCCCGCGTCTCCTCCGCTGCCCTGGCCCTTCCAC
CAACTCCAACCTCTTCTCCCTCCAGCTCCACTCGTAGTCCCCGACTCCGCCAGGCCCTGGCCCGCTGCCGTAG
CGCCGCTTCCCGTCCGGTCCAAAGGTGGGAACCGCTCCGCCCGGCCACCAATGGCACGGTTGGCTGCC
CGCGCTTCTCTGACCCCTGGCAGTGCAGCGCCGCGTCTGGCTGCCGAGCTCAAGTCGAAAAGTTGCTCGG
AAGTGCACGTCTTACGTGCTCAAAGGCTCAACAAGAACGATGCCCTCCACCGAGATCAACGGTATCAT
TTGAAGATCTGCCCCAGGGTCTACTGCTGCTCAAGAGATGGAGGAGAAGTACAGCCTGCAAAGTAAAGA
TGATTCAAAAGTGTGGTACGCAACAGTGCAATCATTTGCAAGCTGTCTTGCTTACGTTAACAGAAGTTG
ATGAATTCTCAAAGAACACTTGAAAATGCAAGAGAAATCCCTGAATGATATGTTGTAAGACATATGGCCAT
TTATACATGCAAATCTGAGCTATTAAAGATCTCTCGTAGAGTTGAAACGTTACTACGTTGGGGAAATGT
GAACCTGGAAAGAAATGCTAAATGACTCTGGGCTGCCCTGGAGCGGATGTTCCGCTGGTGAACCTCCAGT
ACCACTTACAGATGAGTATCTGAATGTGACGAAAGTATACGGAGCAGCTGAAGCCCTTCGGAGATGTCCT
CGCAAATTGAAGCTCCAGGTTACTCGTCTTGTAGCAGCCGTAAGGCTTACGCTCAAGGCTTAGCGGTTGC
AGATGTCGTGAGCAAGGTCTCGTGGAAACCCCCACAGCCCAGTGTACCCATGCCCTGGTGAAGATGATCTACT
GCTCCCACTGCCGGGGTCTCGTACTGTGAAGCCATGTTACAACACTACTGCTCAAACATCATGAGAGGGCTGTTG
GCCAACCAAGGGGATCTGATTTGAATGGAACAATTCTAGATGCTATGCTGATGGTGGCAGAGAGGCTAGA
GGGCTTTCAACATTGAATCGTCATGGATCCCATCGATGTGAAGATTCTGATGCTATTATGAACATGCAGG
ATAATAGTGTCAAGTGTCTCAGAAGGTTTCCAGGGATGTGGACCCCCCAAGCCCTCCAGCTGGACGAATT
TCTCGTTCCATCTGAAAGTGCCTTCAGTGCCTCAGACCACATCACCCCGAGGAACGCCAACACAGC
AGCTGGCACTAGTTGGACCGACTGGTACTGATGTCAGGAGAACTGAAACAGGCCAAGAAATTCTGGTCT
CCCTCCGAGCAACGTTGCAACGATGAGAGGATGGCTCAGGAAACGCCAATGAGGATGACTGTTGGAAATGG
AAAGGCAAAGCAGGTACCTGTCAGTGACAGGAAATGGATTAGCCAACAGGGCAACAACCCAGAGGCTCA
GGTGACACCAGCAAACGACATACTGATCCTCGTCAAATCATGGCTTCTCGAGTGTGATGACCAGCAAGATGA
AGAATGCATACAATGGGAACGACGTGGACTTCTGATATCAGTGTGATGAAAGTAGTGGAGAAGGAAGTGGAA
GGCTGTGAGTATCAGCAGTGCCTTCAGAGTTGACTACAATGCCACTGACCATGCTGGAGAGGTGCCAATGA
GAAAGCCGACAGTGTGGTGTCCGTCTGGGACAGGCCAACCTCTCACTGTTCTGCATCTGTTGG
TTATGCAGAGAGAGTGGAGATAATTCTCAAACCTCTGAGAAAAAGTGTCTCATAAAAAGTTAAAAGGCACCAGTT
ATCACTTTCTACCATCCTAGTGTACTTGTCTTAAATGAATGGACAACATGTACAGTTTACTATGTGGC
CACTGGTTAAAGAAGTGTGACTTTGTCTTCAATTGAGTTGGAGGAAAGGGACTGTGCATTGAGTTGGT
TCCCTGCTCCCCAACATGTTAACGTGGTAACAGTGTAGGTACAGAACTATAGTTAGTTGTGCATTGTGA
TTTATCACTCTATTATTTGTGTATGTTTCTCATTTGTTGTGGTTTTTTTCAACTGTGATCT
CGCTTGTCTTACAAGCAAACCGGGTCCCTTGTGGCACGTAACATGTACGTATTCTGAAATATTAAATA
GCTGTACAGAAGCAGGTTTATTATGTTATCTTAAAGAAAAGCCAAAAAGC

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FIGURE 97

MARFGLPALLCTLAVLSAALLAAELKSKSCSEVRRLYVSKGFNKNDAPLHEINGDHLKICPQ
GSTCCSQEMEEKYSLQSKDDFKSVVSEQCNHLQAVFASRYKKFDEFFKELLENAEKSNDMF
VKTYGHLYMQNSELFKDLFVELKRYYVVGVNLEEMLNDFWARLLERMFRLVNSQYHFTDEY
LECVSKYTEQLKPGDVRKLKLQVTRAFVAARTFAQGLAVAGDVSKVSVNPTAQCTHAL
LKMIYCSHCRLVTVKPCNYCSNIMRGCLANQGDLDFEWNNFIDAMILMVAERLEGPFNIES
VMDPIDVKISDAIMNMQDNSVQVSQKVFQGCGPPKPLPAGRISRSISESAFSARFRPHHPEE
RPTTAAGTSLDRLVTDVKEKLKQAKKFSSLPSNCNDERMAAGNGNEDDCWNGKGKSRYLF
AVTGNGLANQGNNPEVQVDTSKPDILILRQIMALRVMTSKMKNAYNGNDVDFFDISDESSGE
GSGSGCEYQQCPSEFDYNATDHAGKSANEKADSAGVRPGAQAYLLTVFCILFLVMQREWR

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FIGURE 98

CTCGCCCTCAAATGGGAACGCTGGCCTGGACTAAAGCATAGACCACCAGGCTGAGTATCCT
GACCTGAGTCATCCCCAGGGATCAGGAGCCTCCAGCAGGGAACCTCATTATATTCTTCAA
GCAACTTACAGCTGCACCGACAGTTGCGATGAAAGTTCTAATCTTCCCTCCTGTTGC
TGCCACTAATGCTGATGTCCATGGTCTCTAGCAGCCTGAATCCAGGGTGCAGAGGCCAC
AGGGACCGAGGCCAGGCTTAGGAGATGGCTCCAGGAAGGCCAAGAATGTGAGTGCAA
AGATTGGTTCTGAGAGGCCCGAGAAGAAAATTCAAGGGCAATGTGAAGAAAACAAGACACCAAGGCACCACAGA
AGTGCCCTGTGATCATTCAAGGGCAATGTGAAGAAAACAAGACACCAAGGCACCACAGA
AAGCCAAACAAGCATTCCAGAGCCTGCCAGCAATTCTCAAACAATGTCAGCTAAGAAGCTT
TGCTCTGCCTTGTAGGAGCTCTGAGCGCCCACTCTTCCAATTAAACATTCTCAGCCAAGAA
GACAGTGAGCACACCTACCAAGACACTCTTCTCCACCTCACTCTCCACTGTACCCACC
CCTAAATCATTCCAGTGCTCTCAAAAGCATGTTTCAAGATCATTGTTGCTCTC
TCTAGTGTCTTCTCTCGTCAGTCTTAGCCTGTGCCCTCCCTACCCAGGCTTAGGCTT
AATTACCTGAAAGATTCCAGGAAACTGTAGCTCCTAGCTAGTGTCAATTAAACCTAAATGC
AATCAGGAAAGTAGCAAACAGAAGTCAATAATATTAAATGTCAAAAAAAAAAAAAAA

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FIGURE 99

MKVLISLLLLPLMLMSMVSSLNPGVARGHRDRGQASRRWLQEGGQECECKDWFLRAPRR
KFMTVSGLPKKQCPCDHFKGNVKKTRHQRHHRKPNKHSRACQQFLKQCQLRSFALPL

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FIGURE 100

AATGGCTGTCTTAGTACTTCGCCTGACAGTTGCTGGACTGCTTGTCTATTCCGTACCT
GCTATGCAGACGACAAACCAGACAAGCCAGACGACAAGCCAGACGACTCAGGCAAAGACCCA
AAGCCAGACTTCCCCAAATTCTAAAGCCTCTGGCACAGAGATCATTGAGAATGCAGTCGA
GTTCATCCTCCGCTCCATGTCCAGGAGCACAGGATTATGGAATTGATGATAATGAAGGAA
AACATTCAAAAGTGACATCCTCAGGACACACCCATGTGGCTCTGGACAATCCAAGAGCA
GCCAAATCCTGCTTTCCAGTTGGCTCCACAAGTCCTCCAGGACAGAGCCCTAAAGCAAC
TCCCAACGAGTTCTCAGGATTCAAGGCTCTGGCTCAACCAAACAGAACTCATTGAAACACC
CTGACTGCATTTGCTTTAGAAAGTTAGAATAATGGCGCTTGGATCACATAGTTG
ATGGAGAGGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 101

MAVLVLRLTVVLGLLVLFLTCYADDKPDKPDDKPDMSGKDPKPDFPKFLSLLGTEIIENAVE
FILRSMSRSTGFMEFDDNEGKHSSK

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FIGURE 102

GGACGCCAGCGCCTGCAGAGGCTGAGCAGGGAAAAAGCCAGTCCCCAGCGGAAGCACAGCT
CAGAGCTGGTCTGCCATGGACATCCTGGTCCCACTCCTGCAGCTGCTGGTCTGCTTCTAC
CCTGCCCTGCACCTCATGGCTCTGCTGGCTGCTGGCAGCCCCTGTGCAAAAGCTACTTCC
CCTACCTGATGGCGTGCTGACTCCAAAGAGCAACCGCAAGATGGAGAGCAAGAAACGGGAG
CTCTTCAGCCAGATAAAAGGGCTTACAGGAGCCTCCGGAAAGTGGCCCTACTGGAGCTGGG
CTGCGGAACCGGAGCCAACTTCAAGTCTACCCACCGGGTGCAGGGTCACCTGCCAGACCC
CAAATCCCCACTTGAGAAGTTCTGACAAAGAGCATGGCTGAGAACAGGCACCTCCAATAT
GAGCGGTTGTGGTGGCTCCTGGAGAGGACATGAGACAGCTGGCTGATGGCTCCATGGATGT
GGTGGTCTGCACTCTGGTGTGCTGTGCTGAGAGCCAAAGGAAGGTCTGCAGGGAGGTCC
GGAGAGTACTGAGACCGGGAGGTGTGCTTTCTGGAGCATGTGGCAGAACCATATGGA
AGCTGGCCTTCATGTGGCAGCAAGTTCTGAGCCCACCTGGAAACACATTGGGATGGCTG
CTGCCTCACCAAGAGAGACCTGGAAGGATCTTGAGAACGCCAGTTCTCCGAAATCCAAATGG
AACGACAGCCCCCTCCCTGAAGTGGTACCTGTTGGCCCCACATCATGGAAAGGCTGTC
AAACAATCTTCCAAGCTCCAAGGCACACTCATTGCTCCTCCCCAGCCTCCAATTAGAAC
AGCCACCCACCAGCCTATCTATCTTCACTGAGAGGGACTAGCAGAACATGAGAGAACATT
CATGTACCACTACTAGTCCCTCTCTCCCCAACCTCTGCCAGGGCAATCTCTAACATTCAATC
CCGCCTCGACAGTGGAAAAAGCTCTACTTCTACGCTGACCCAGGGAGGAAACACTAGGACCC
TGTGTATCCTCAACTGCAAGTTCTGGACTAGTCTCCAACGTTGCCTCCAAATGTTGTC
CCTTCCTCGTCCATGGTAAAGCTCCTCTGCCCTCTGAGGCTACACCCATGCGT
CTCTAGGAACCTGGTCAAAAAGTCATGGTGCCTGCATCCCTGCCAACGCCCTGACCCCT
CTCCCCACTACCACCTCTGCCAGCTGGGGCACCAGGGAGAACATGAGATGCTGGGAT
GCCAGAGCAAGACTCAAAGAGGCAGAGGTTTGTCTCAAATATTTTAATAAATAGACGA
AACCAAG

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FIGURE 103

MDILVPLLQLLVLLLTLPLHLMALLGCWQPLCKSYFPYLMAVLTPKSNRKMESKKRELFSQI
KGLTGASGKVALLELGCGTGANFQFYPPGCRVTCLDPNPHFEKFLTKSMAENRHLQYERFVV
APGEDMRQLADGSMDVVVCTLVLCVQSPRKVLQEVRVLRPGGVLFWEHVAEPYGSWAFM
WQQVFEPTWKHIGDGCCLTRETWKDLENAQFSEIQMERQPPPLKWLPGPHIMGKAVKQSFP
SSKALICSFPSLQLEQATHQPIYLPLRGT

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FIGURE 104

GTGGGATTATTGAGTGCAAGATCGTTCTCAGGGGGAGTTGCCTCATGCAGG
CAGATGTTGGGCTTGTCCGAACAGCTCCCTCTGCCAGCTCTGTAGATAAGGGTTAAA
ACTAATATTATATGACAGAAGAAAAGATGTCATTCCGTAAAGTAAACATCATCATCTTGG
TCCTGGCTGTTGCTCTCTTACTGGTTGCACCATAACTCCTCAGCTGAGCAGTTG
TTAAGGAATGAGGTTACAGATTCAAGGAATTGTAGGGCCTAACCTATAGACTTGTCCAAA
TGCTCTCCGACATGCAGTAGATGGAGACAAGAGGAGATTCCGTGGTCATCGCTGCATCTG
AAGACAGGCTGGGGGGCCATTGCAGCTATAAACAGCATTCAAGCACAACACTCGCTCCAAT
GTGATTTCTACATTGTTACTCTCAACAATACAGCAGACCATCTCCGGCCTGGCTAACAG
TGATTCCCTGAAAGCATCAGATACAAAATTGTCAATTGACCCCTAAACTTTGGAAGGAA
AAGTAAAGGAGGATCCTGACCAGGGGAATCCATGAAACCTTAACCTTGCAAGGTTCTAC
TTGCCAATTCTGGTTCCAGCGCAAAGAAGGCCATATACATGGATGATGATGTAATTGTGCA
AGGTGATATTCTGCCCTTACAATACAGCACTGAAGCCAGGACATGCAGCTGCATTTCAG
AAGATTGTGATTGCCTACTAAAGTTGTCATCCGTGGAGCAGGAAACCAGTACAATTAC
ATTGGCTATCTGACTATAAAAGGAAAGAATTGTAAGCTTCCATGAAAGCCAGCACTG
CTCATTAACTCCTGGAGTTTGTCAAACCTGACGGAATGGAAACGACAGAATATAACTA
ACCAACTGGAAAATGGATGAAACTCAATGTAGAAGAGGGACTGTATAGCAGAACCTGGCT
GGTAGCATCACAAACACCTCCTGCTTACGCTTATCGTATTTCACAGCACTCTACCATCGATCC
TATGTGGAATGTCCGCCACCTGGTTCCAGTGCTGGAAAACGATATTCACCTCAGTTGTAA
AGGCTGCCAAGTTACTCCATTGGAATGGACATTGAAAGCCATGGGAAGGACTGCTTCATAT
ACTGATGTTGGAAAAATGGTATATTCCAGACCCAAACAGGAAATTCAACCTAACCGAAG
ATATAACCGAGATCTCAAACATAAAGTGAAACAGAATTGAACTGTAAGCAAGCATTCTCAG
GAAGTCCTGGAAAGATAGCATGGAAAGTAACAGTTGCTAGGCTTCAATGCCATCGGT
GCAAGCCATGGAAAAGATGTGTCAGCTAGGTAAAGATGACAAACTGCCCTGTGGCAGTC
AGCTTCCCAGACAGACTATAGACTATAAAATATGTCCTCATGCCCTACCAAGTGTGTTCTT
ACTACAATGCTGAATGACTGGAAAGAAGAACTGATATGGCTAGTCAGCTAGCTGGTACAGA
TAATTCAAACACTGCTGTTGGTTAATTGTAACCTGTGGCCTGATCTGTAATAAAACTT
ACATTTC

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FIGURE 105

MSFRKVNIILVLAVALFLLVLHHNFLSLSLLRNEVTDSGIVGPQPIDFVPNALRHAVDGR
QEEIPVVIASEDRLGGAIAAINSIQHNTRSNVIFYIVTLNNNTADHLRSWLNSDSLKSIRYK
IVNFDPKLLEGKVKEDPDQGESMKPLTFARFYLPILVPSAKKAIYMDDDVIVQGDILALYNT
ALKPGHAAAFSEDCDASTKVVIRGAGNQNYIGYLDYKKERIRKLSMKASTCSFNPGVFVA
NLTEWKRNQITNQLEKWMKLNVEEGLYSRTLAGSITTPPLLIVFYQQHSTIDPMWNVRHLGS
SAGKRYSPQFVKAAKLLHWNGHLKPWGRTASYTDVWEKWYIPDPTGKFNLIRRYTEISNIK

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FIGURE 106

TGGTTTTGCCCATAAATTCCCTCAGCTTGAGCAGTTGTTAAGGAATGAGGTTACAGATT
CAGGAATTNTAGGNCCCTAACCTNTAGANTTGTCCCAAATGTTCTCCGACATGCAGTAGAT
GGGAGACAAGAGGAGATTCCCTGTGGTCATCGCTGCATNTGAAGACAGGCTGGGGGGCCAT
TGCAGCTATAAACACGCATTCAAGCACAACACTCGNTCCAATGTGATTTCTACATTGTTACTC
TCAACAATACAGCAGACCATNTCCGGTCTGGNTCAACAGTGATTCCCTGAAAAGCATCAGA
TACAAAATTGTCATTTGACCCCTAAACCTTGGAGGGAAAAGTAAAGGAGGATCCTGACCA
GGGGGAATCCATGAAACCTTAACCTTGCAAGGTTCTACTGCCAATTCTGGTTCCCAGCG
CAAAGAAGGCCATATACATGGATGATGTAATTGTGCAAGGTGATATTCTTGCCTTAC
AATACAGCACTGAAGCCAGGACATGCAGCTGCATTTCAGAAGATTGTGATTCAAGCCTCTAC
TAAAGTTGTCATCCGTGGAGCAGGAAA

FIGURE 107

CGACGCTCTAGCGGTTACCGCTGCAGGCTGGCTGGCGTAGTGGGCTGCGCGGCTGCCACG
GAGCTAGAGGGCAAGTGTGCTCGGCCAGCGTGAGGAACGCGGCGGCCAGACAAACGGGC
TGGGCTCCGGGGCCTGCGCGCGGCGTAGCTGGCAGGGCGGGTGGGGCGCGGGCTGCA
TCCGATCTCCTCCATCGCCTGCAGTAAGGGCGGCCGCGGAGCCTTGAGGGAAACGACT
TGTGGAGCCCTAACCAAGGGGTGTCTCTGAGCCTGGTGGATCCCCGGAGCGTCACATCACT
TTCCGATCACTCAAAGTGGTAAAAACTAATATTATATGACAGAAGAAAAAGATGTCATT
CCGTAAGTAAACATCATCATCTTGGTCTGGCTGTTGCTCTTCTACTGGTTTGAC
CATAACTCCTCAGCTTGAGGCAGTTGTTAAGGAATGAGGTTACAGATTAGGAATTGAG
GGCCTCAACCTATAGGACTTGTCCAAATGCTCTCGACATGCAGTAGATGGGAGACAAGA
GGAGATTCTGTGGTCATCGCTGCATCTGAAGACAGGCTGGGGGGCATTGAGCTATAA
ACAGCATTCAAGCACAACACTCGCTCCAATGTGATTTCACATTGTTACTCTCAACAATACA
GCAGACCATCTCCGGTCTGGCTAACAGTGATTCCCTGAAAAGCATCAGATAACAAATTG
TCAATTGACCCCTAAACTTTGAAAGGAAAGTAAAGGAGGATCCTGACCAGGGGAATCC
ATGAAACCTTAACCTTGCAAGGTTCTACTTGCCAATTCTGGTCCAGCGCAAAGAAGG
CCATATACATGGATGATGATGAAATTGTGCAAGGTGATATTCTGCCCTTACAATACAGCA
CTGAAGCCAGGACATGCAGCTGCATTTCAGAAGATTGTGATTCAAGCTACTAAAGTTG
CATCCGTGGAGCAGGAAACCAGTACAATTACATTGGCTATCTGACTATAAAAGGAAAGAA
TTCGTAAGCTTCCATGAAAGCCAGCACTTGCTCATTAATCCTGGAGTTTGCAAC
CTGACGGAATGGAAACGACAGAATATAACTAACCAACTGGAAAAATGGATGAAACTCAATGT
AGAAGAGGGACTGTATAGCAGAACCTGGCTGGTAGCATCACACACCTCCTGCTTATCG
TATTTTATCAACAGCACTTACCATCGATCCTATGTGGATGTCCGCCACCTGGTTCCAGT
GCTGGAAAACGATATTCACCTCAGTTGAAAGGCTGCCAGTTACTCCATTGGATGGACA
TTTGAAGCCATGGGAAGGACTGCTTACATACTGATGTTGGGAAAATGGTATATTCCA
GACCCAAACAGGCAAATTCAACCTAACCGAAGATACCGAGATCTCAAACATAAAAGTGAAA
CAGAATTGAACTGTAAGCAAGCATTCTCAGGAAGTCCTGGAAGATAGCATGCGTGGGAAG
TAACAGTTGCTAGGCTCAATGCCATCGGTAGCAAGCCATGGAAAAAGATGTGTCAGCTAG
GTAAAGATGACAAACTGCCCTGTCTGGCAGTCAGCTCCAGACAGACTATAGACTATAAAT
ATGTCCTCATCTGCCATTACCAAGTGTGTTCTACTACAATGCTGAATGACTGGAAAGAAGAA
CTGATATGGCTAGTTCAGCTAGCTGGTACAGATAATTCAAAACTGCTGTTGGTTAATT
GTAACCTGTGGCCTGATCTGAAATAAAACTACATTCAATAGGTAAAAAAAAAAAAAA
AAAAAA

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FIGURE 108

CTGCAGGTAGACATCTCACTGCCAGGAATCACTGAGCGTGCAGACAGCACAGCCTCCTCT
GAAGGCCGCCATACCAAGACTCCTGCCTCGGCATGGGCCTCACCATGGAGGCAGCTCCACTG
TCTGTGCTGGTCTGAGGGTGCTGCCTGTC**ATGGGGCAGCCATCTCCCAGGGGCCCTCATC**
GCCATCGTCTGCAACGGTCTCGTGGCTTCTGCTGCTGCTCTGGTCATCCTCTGCTG
GGCCTGCCATTCTCGTCTGCCGACGTTGACTCTCTCTGAATCCAGTCCAACTCCAGCCC
TGGCCCTGCTGAGAAGGCCCCACCACCCAGAAGCCCAGCCATGAAGGCAGCTACCTGC
TGCAGCCCTGAAGGCCCCCTGGCCTAGCCTGGAGGCCAGGAC**TAA**GTCCACCTCACCTAGAG
CCTGGAATTAGGATCCCAGAGTTAGCCAGCCTGGGTCCAGAACTCAAGAGTCCGCCTGCT
TGGAGCTGGACCCAGCGGCCAGACTAGCCAGCTGGCTCCAATAGGAGCTAGTGGCCC
TAAGGAGATGGCCTGGGTGGGGCTTATGAGTTGGTGCTAGGCCAGGGCCATCTGGACT
ATGCTCCATCCCAAGGGCAAGGGTCAGGGCCGGGTCCACTCTTCCTAGGCTGAGCACC
TCTAGGCCCTCTAGGTTGGGAAGCAAACCTGGAACCCATGGCAATAATAGGAGGGTGTCCAG
GCTGGGCCCTCCCTGGCCTCCAGTGGTTGCTGGATAATAATGGAACTATGGCTCTAA
AAAAAAAAAAAAAA

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FIGURE 109

MGAAISQGALIAIVCNGFLLLLWVILCWACHSRLPTLTLNPNVPTPALAPVLRRPHH
PRSPAMKAATCCSPEGPWPSLEPRT

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FIGURE 110

GTTCGAATTCTTCAACTATACCCACAGTCCAAAGCAGACTCACTGTGTCCCAGGCTACCA
GTTCCCTCCAAGCAAGTCATTCCTTATTAAACGATGTGTCCCTCAAACACCTGAGTGCTA
CTCCCTATTGCATCTGTTGATAATGATGTTGACACCCTCCACCGAATTCTAAGTGGAA
TCATGTGCGGAAGAGATAACAATCCTGGCCTGTGTATCCTCGCATTAGCCTGTCTTGGCC
ATGATGTTACCTTCAGATTCATCACCACCCCTCTGGTCACATTTCATTCATTGGTTAT
TTTGGGATTGTTGTTGTCTGCGGTGTTATGGTGGCTGTATTATGACTATACCAACGACC
TCAGCATAGAATTGGACACAGAAAGGGAAAATATGAAGTGCCTGCTGGGTTGCTATCGTA
TCCACAGGCATCACGGCAGTGCTCGTCTTGATTTGTTCTCAGAAAGAGAATAAAATT
GACAGTTGAGCTTCCAAATCACAAATAAGCCATCAGCAGTGCTCCCTCCTGCTGTTCC
AGCCACTGTGGACATTGCCATCCTCATTTCTGGTCCTCTGGGTGGCTGTGCTGCTG
AGCCTGGGAACTGCAGGAGCTGCCAGGTTATGGAAGGGCGGCCAAGTGAATATAAGCCCCT
TTCGGGCATTGGTACATGTGGTCGTACCTTAATTGGCCTCATCTGGACTAGTGAATTCA
TCCTTGCCTGCCAGCAAATGACTATAGCTGGGCAGTGGTTACTTGTATTCAACAGAAGT
AAAAATGATCCTCCTGATCATCCCATCCTTCGTCTCTCCATTCTCTTCTTACCATCA
AGGAACCGTTGTGAAAGGGTCATTTTAATCTCTGTGGTGAGGATTCCGAGAACATCATTGTCA
TGTACATGCAAAACGCACTGAAAGAACAGCAGCATGGTCATTGTCCAGGTACCTGTTCCGA
TGCTGCTACTGCTGTTCTGGGTCTTGACAAATACCTGCTCCATCTCAACCAGAACATGCATA
TACTACAACGTCTATTAAATGGGACAGATTCTGTACATCAGAAAAGATGCATTCAAAATCT
TGTCCAAGAACTCAAGTCACTTACATCTATTAACTGCTTGAGACTTCATAATTCTA
GGAAAGGTGTTAGTGGGTGTTCACTGTTGGAGGACTCATGGCTTTAACTACAATCG
GGCATTCCAGGTGTGGCAGTCCTCTGTTATTGGTAGCTTTGCCTACTTAGTAGCCC
ATAGTTTTATCTGTGTTGAAACTGTGCTGGATGCACCTTCCTGTGTTGCTGTGAT
CTGGAAACAAATGATGGATCGTCAGAAAAGCCCTACTTATGGATCAAGAATTCTGAGTT
CGTAAAAGGAGCAACAAATTAAACAATGCAAGGGCACAGCAGGACAAGCACTCATTAAGGA
ATGAGGAGGAAACAGAACACTCCAGGCCATTGTGAGATAGATACCCATTAGGTATCTGTACCT
GGAAAACATTCTCTAAGAGCCATTACAGAATAGAAGATGAGACCAGTAGAGAAAAGTT
AGTGAATTTTTTAAAAGACCTAATAAACCTATTCTCCTCAAAA

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FIGURE 111

MSGRDTILGLCILALALSLAMMFTFRFITTLLVHIFISLVLGLLFVCGVLWWLYYDYTNDL
SIELDTERENMKCVLGFAIVSTGITAVLLVLIFVLRKRIKLTVELFQITNKAISAPFLFQ
PLWTFAILIFFWVLWAVLLSLGTAGAAQVMEGGQVEYKPLSGIRYMWSYHЛИWTSEFI
LACQQMTIAGAVVTCYFNRSKNPDPDHPISSLSILFFYHQGTVVKGFLISVVRIPRIIVM
YMQNALKEQQHGALSRYLFRCYCFCWCLDKYLLHLNQNAYTTAINGTDFCTSAKDAFKIL
SKNSSHFTSINCFGDFIIFLGKVLVVCFTVFGGLMAFNYNRAFQVWAVPLLVAFFAYLVAH
SFLSVFETVLDALFLCAVDLETNDGSSEKPYFMDQEFLSFVKRSNKLNNARAQQDKHSLRN
EEGTELQAIVR

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FIGURE 113

MRTVVLTMKASVIEMFLVLLVTGVHSNKETAKKIKRPKFTVPQINCDVKAGKIIDPEFIVKC
PAGCQDPKYHVYGTDVYASYSSVCGAAVHSGVLDNSGGKILVRKVAGQSGYKGSYSNGVQSL
SLPRWRESFIVLESKPKKGVTPSALTYSSSKSPAAQAGETTKAYQRPIP GTTAQPVTLMQ
LLAVTVAVATPTTLPRPSA STTSIPRPQSVGHRSQEMDLWSTATYTSSQNRPADPGIQ
RQDPSGAAFQKPGADVSLGLVPKEELSTQSLEPVSLGDPNCKIDLSFLIDGSTSIGKRRFR
IQKQLLADVAQALDIGPAGPLMGVVQYGDNPATHFNLKHTNSRDLKTAIEKITQRGGLSNV
GRAISFVTKNFFSKANGNRSGAPNVVVVMVDGWPTDKVEEASRLARESGINIFFITIEGAAE
NEKQYVVEPNFANKAVCRTNGFYSLHVQSWFGLHKTQPLVKRVCDTRLACSKTCLNSADI
GFVIDGSSSGTGNFRTVLQFVTNLTKFEISDTDTRIGAVQYTYEQRLEFGFDKYSSKPDI
LNAIKRVGWSSGTSTGAAINFQLEQLFKKS KPNKRKLMILITDGRSYDDVRI PAMA AHLKG
VITYAIGVAWAAQEELEVIATHPARDHSFFVDEFDNLHQYVPRII QNICTEFNSQPRN

FIGURE 114

CAGGATGAACTGGTTGCAGTGGCTGCTGCTGCGGGGGCGCTGAGAGGACACGAGCTCTA
TGCCTTCCGGCTGCTCATCCCGCTGGCCTCCTGTGCGCGCTGCTGCCTCAGCACCATGGT
GCGCCAGGTCCCGACGGCTCCGCGCCAGATCCGCCACTACAGTTTCTCTGACTCTAAT
TGATGCACTGGACACCTTGCTGATTTGGGAATGTCTCAGAATTCAAAGAGTGGTTGAAG
TGCTCCAGGACAGCGTGGACTTGATATTGATGTGAACGCCTCTGTGTTGAAACAAACATT
CGAGTGGTAGGAGGACTCCTGCTCATCTGCTCTCCAAGAAGGCTGGGTGGAAGTAGA
GGCTGGATGCCCTGTTCCGGCCTCTCCTGAGAATGGCTGAGGAGGCCCGAAAACCTCC
TCCCAGCCTTCAGACCCCCACTGGCATGCCATATGGAACAGTGAACCTTACTTCATGGCGTG
AACCCAGGAGAGACCCCTGTCACCTGTACGGCAGGGATTGGACCTTCATTGTTGAATTGC
CACCTGAGCAGCCTCACTGGTGAACCGGTGTTGAAGATGTGCCAGAGTGGCTTGATGC
GCCCTGGGAGAGCCGGTCAGATATGGCTGGTGGCAACCACATTGATGTGCTCACTGGC
AAAGTGGGTGGCCCAGGACGCAGGCATCGGGCTGGCGTGGACTCCTACTTGAGTACTTGGT
GAAAGGAGCCATCCTGCTTCAGGATAAGAAGCTCATGCCATGTTCTAGAGTATAACAAAG
CCATCCGGAACTACACCCGCTTCGATGACTGGTACCTGTGGGTTAGATGTACAAGGGACT
GTGTCCATGCCAGTCTTCAGTCCTGGAGGCCTACTGGCCTGGTCTTCAGAGCCTCATTGG
AGACATTGACAATGCCATGAGGACCTTCCTCAACTACTACACTGTATGGAAGCAGTTGGG
GGCTCCCGGAATTCTACAACATTCCCTAGGGATAACACAGTGGAGAAGCGAGAGGGCTACCCA
CTTCGGCCAGAACTTATTGAAAGCGCAATGTACCTTACCGTGCCACGGGGATCCCACCC
CCTAGAACTCGGAAGAGATGCTGTGAATCCATTGAAAAAAATCAGCAAGGTGGAGTGCAGGAT
TTGCAACAATCAAAGATCTGCGAGACCACAAGCTGGACAACCGCATGGAGTCGTTCTCCTG
GCCGAGACTGTGAAATACCTTACCTCTGGTTGACCCAAACCAACTTCATCCACAATGG
GTCCACCTCGACGCCGTGATCACCCCTATGGGAGTGCATCCTGGGGCTGGGGGTACA
TCTTCAACACAGAAGCTCACCCATCGACCTTGCCGCCCTGCACTGCTGCCAGAGGCTGAAG
GAAGAGCAGTGGGAGGTGGAGGACTTGATGAGGAAATTCTACTCTCAAACGGAGCAGGT
GAAATTTCAGAAAAACACTGTTAGTTGGGGCATGGAACCTCCAGCAAGGCCAGGAACAC
TCTTCTCACCAGAAAACCATGACCAGGCAAGGGAGAGGAAGCCTGCCAAACAGAAGGTCCA
CTTCTCAGCTGCCAGTCAGCCCTCACCTCCAAGTTGGCATTACTGGACAGGTTTCT
AGACTCCTCATAACCACTGGATAATTTTTATTTTGTAGGCTAAACTATAATA
AATTGCTTTGGCTATCATAAAA

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FIGURE 115

MPFRLLIPLGLLCALLPQHHGAPGPDGSAPDPAHYSFSLTLIDALDTLLILGNVSEFQRVVE
VLQDSVDFDIDVNASVFETNIRVVGGLSAHLLSKKAGVEVEAGWPCSGPLLRLMAEEAARKL
LPAFQTPTGMPYGTVNLLHGVNPGETPVTCTAGITFIVEFATLSSLTGDPVFEDVARVALM
RLWESRSIDGLVGNHIDVLTGKWVAQDAGIGAGVDSYFEYLVKGAILLQDKKLAMFLEYNK
AIRNYTRFDDWYLWVQMYKGTVSMPVFQSLEAYWPGLQSLIGDIDNAMRTFLNYYTVWKQFG
GLPEFYNIQPQGYTVEKREGYPLRPELIESAMYLYRATGDPTLLELGRDAVESIEKISKVECG
FATIKDLRDHKLDNRMESFFLAETVKYLYLLFDPTNFIHNNGSTFDAVITPYGECILGAGGY
IFNTEAHPIDLAALHCCQRLKEEQWEVEDLMREFYSLKRSRSKFQKNTVSSGPWEPPARPGT
LFSPENHDQARERKPAKQKVPLLSCPSQPFITSKLALLGQVFLDSS

FIGURE 116

AAAGTTACATTTCTCTGGAACCTCCTAGGCCACTCCCTGCTGATGCAACATCTGGTTG
GGCAGAAAGGAGGGTGCTCGGAGCCCGCCCTTCTGAGCTCCTGGGCCGGCTAGAACAA
ATTCAGGCTCGCTCGACTCAGACCTCAGCTCCAACATATGCATTCTGAAGAAAGATGGCT
GAGATGGACAGAACATGCTTATTGGAAAGAACATGTTCTAGGTCAAACGTGAGTCTACCA
AATGCAGACTTCACAATGGTTCTAGAAGAACATCTGGACAAGTCTTCATGTGGTTTTCT
ACGCATTGATTCCATGTTGCTCACAGATGÁAGTGGCATTCTGCCTGCCCTCAGAACCTC
TCTGTACTCTCAACCAACATGAAGCATCTTGATGTGGAGCCCAGTGATCGGCCCTGGAGA
AACAGTGTACTATTCTGTCGAATACCAAGGGGAGTACGAGAGCCTGTACACGAGCCACATCT
GGATCCCCAGCAGCTGGTGCTCACTCACTGAAGGTCCTGAGTGTGATGTCACTGATGACATC
ACGCCACTGTGCCATACAACCTCGTGTCAAGGCCACATTGGCTCACAGACCTCAGCCTG
GAGCATCCTGAAGCATCCCTTAATAGAACACTCAACCATCCTAACCGACCTGGGATGGAGA
TCACCAAAGATGGCTCCACCTGGTATTGAGCTGGAGGACCTGGGCCAGTTGAGTTC
CTTGTGGCCTACTGGAGGAGGGAGCCTGGTGCCAGGAACATGTCAAAATGGTGAGGAGTGG
GGGTATTCCAGTGCACCTAGAAACCATGGAGCCAGGGCTGCATACTGTGTAAGGCCAGA
CATTGTAAGGCCATTGGAGGTACAGCGCTTCAGCCAGAACATGTGTGGAGGTGCAA
GGAGAGGCCATTCCCTGGTACTGGCCTGTTGCCTTGTGGCTCATGCTGATCCTGT
GGTCGTGCCACTGTTCGTCTGGAAAATGGCCGGCTGCTCCAGTACTCCTGTTGCCCGTGG
TGGCCTCCCAGACACCTTGAAAATAACCAATTACCCCCAGAAGTTAACAGCTGCAGAAGG
GAGGAGGTGGATGCCGTGCCAGGTGAAGCCAGAACCTGGTCTGCATGACATGGAAACC
CTCAT**AGGT**TTGCCAGGGCCAGGTGAAGCCAGAACCTGGTCTGCATGACATGGAAACC
ATGAGGGACAAGTTGTTCTGTTTCCGCCACGGACAAGGGATGAGAGAACAGTAGGAAGA
GCCTGTTGTCACAAGTCTAGAACGCAACCATCAGAGGCAGGGTGGTTGTCTAACAGAACAC
TGACTGAGGCTTAGGGATGTGACCTCTAGACTGGGGCTGCCACTGCTGGCTGAGCAACC
CTGGAAAAGTGACTTCATCCCTCGGTCTAACGTTCTCATCTGTAATGGGAAATTACC
TACACACCTGCTAACACACACACAGAGTCTCTCTATATACACACGTACACATAAA
TACACCCAGCACTTGCAAGGCTAGAGGGAAACTGGTACACTCTACAGTCTGACTGATTGAG
TGTTCTGGAGAGCAGGACATAATGTATGATGAGAACATCAAGGACTCTACACACTGGGT
GGCTTGGAGAGCCCACTTCCAGAATAATCCTTGAGAGAAAAGGAATCATGGAGCAATGG
TGTGAGTTCACTTCAAGCCCAATGCCGGTGCAGAGGGGAATGGCTTAGCGAGCTCTACAGT
AGGTGACCTGGAGGAAGGTACAGCCACACTGAAAATGGATGTGCATGAACACGGAGGATC
CATGAACTACTGTAAAGTGTGACAGTGTGCACACTGCAGACAGCAGGTGAAATGTATGT
GTGCAATGCGACGAGAACATGCAGAACGTCAAGTACATGTGCATGTTGTTGCTCCTTTTC
TGTGGTAAAGTACAGAACATTCAAGCAAATAAAAGGCCACCTGGCAAAAGCGGTAAAAAA
AAAAAAAAAA

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FIGURE 117

MQTFTMVLEEIWTSLFMWFFYALIPCLLTDEVAILPAPQNLSQLSTNMKHLLMWSPVIAPGE
TVYYSVEYQGEYESLYTSHIWIPSSWCSILTEGPECVDVTDDITATVPYNLVRATLGSQTSAW
SILKHPFNRNSTILTRPGMEITKDGFLVIELEDLGPQFEFLVAYWRREPGAEHHVKMVRSG
GIPVHLETMEPGAAYCVKAQTFVKAIGRYSAFSQTECVEVQGEAIPLVLALFAFVGFMLILV
VVPLFVWKMGRLLQYSCCPVVVLPTDLKITNSPQKLISCRREEVDACATAVMSPEELLRAWIS

Important features:**Signal peptide:**

amino acids 1-29

Transmembrane domain:

amino acids 230-255

N-glycosylation sites.

amino acids 40-43 and 134-137

Tissue factor proteins homology.

amino acids 92-119

Integrins alpha chain protein homology.

amino acids 232-262

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FIGURE 118

TCCTGCTGATGCACATCTGGTTGGCAAAAGGAGGTTGCTCGAGCCGCCCTTAGCTT
CCTGGCCGGCTCTAGAACAAATTCAAGGCTCGCTCGACTAGACCTCAGCTCCAACATATGCA
TTCTGAAGAAAGATGGCTGAGATGACAGAATGCTTATTTGGAAAGAAACAATGTTCTAGG
TCAAACGTAGTCTACCAAATGCAGACTTCACAATGGTTCTAGAAGAAATCTGGACAAGTCT
TTTCATGTGGTTTCTACGCATTGATTCCATGTTGCTCACAGATGAAGTGGCCATTCTGC
CTGCCCTCAGAACCTCTGTACTCTAACCAACATGAAGCATCTTGTGATGTGGAGCCCA
GTGATCGCCCTGGAGAACAGTGTACTATTCTGTCGAATACCAGGGGAGTACGAGAGCCT
GTACACGAGCCACATCTGGATCCCCAGCAGCTGGTGCCTCACTCACTGAAGGTCTGAGTGTG
ATGTCACTGATGACATCACGGCACTGTGCCATACAACCTTGTGTCAGGGCCACATTGGGC
TCACAGACCTCAGCCTGGAGCATCCTGAAGCATCCCTTAATAGAAACTCAACCATCCTTAC
CCGACCTGGGATGGAGATCACCAAAGATGGCTNCACCTGGTTATTGAGCTGGAGGACCTGG
GGCCCCAGTTGAGTTCTGTGGCCTANTGGAGGAGGGCGAACCCCTGCGCGCAAGGG
GTTNGCGAACCCCTTGCGGCCGCTGGGTATCTCTCGAGAAAAGAGAGGCCAATATGACCCAC
ATACTCAATATGGACGAANTGCTATTGTCCACCTGTTGAGTGGCGCTGGTTGAT

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FIGURE 119

CGGACGCGTGGGCCGCCACCTCCGGAACAAGCCATGGTGGCGGCGACGGTGGCAGCGCGTG
GCTGCTCCTGTGGCTGC~~GG~~C~~T~~GC~~GC~~C~~G~~CAGCAGGAGCAGGACTTCTACGACTTCAGCGG
TCAACATCCGGGGCAAAC~~TGGTGT~~CGCTGGAGAAGTACCG~~GG~~ATCGGTGTC~~CC~~CTGGTGGTG
AATGTGGCCAGCGAGTGC~~GG~~CTTCACAGACCAGCACTACCGAGCC~~T~~GCAGCAGCTGCAGCG
AGACCTGGGCCCCCACCAC~~TT~~AACGTGCTGC~~CC~~TTCC~~CC~~TGCAACCAGTTGCCAACAGG
AGCCTGACAGCAACAAGGAGATTGAGAGCTTGCCGCCAC~~CT~~TACAGTGTCTCATTCCCC
ATGTTAGCAAGATTG~~CAGTCACCGT~~ACTGGTG~~CC~~CATCCTGC~~CT~~CAAGTACCTGG~~CC~~CA
GACTTCTGGGAAGGAG~~CC~~AC~~TG~~AACTCTGGAAAGTACCTAGTAG~~CCC~~CAGATGGAAAGG
TGGTAGGGCTGGGACCCAACTGTGT~~CAGTGGAGGAGGT~~CAGAC~~CC~~CAGATCACAGCGCTC
GTGAGGAAGCTCATC~~CT~~ACTGAAGCGAGAAGACTTATAACCACCG~~GT~~TC~~CT~~CC~~CT~~CCACCA
CCTCATCCC~~CC~~AC~~CT~~GTGTGGGCTGACCAATGCAAAC~~TCAA~~ATGGT~~GCTT~~CAAAGGGAG
AGACCCACTGACTCTC~~CT~~CC~~TT~~ACTCTTATGCCATTGGT~~CC~~CATCATTCTTG~~GGGG~~AA
AAATTCTAGTATTTGATTATTGAATCTTACAGCAACAAATAGGAAC~~T~~C~~CT~~GG~~CC~~AA~~TG~~AG
AGCTCTTGACCAGTGAATCAC~~CA~~CCAGCCGATACGAACGT~~CT~~TGCCAACAAAATGTGTGG~~CC~~AA
TAGAAGTATATCAAGCAATAATCT~~CC~~AC~~CC~~AA~~GG~~CT~~T~~GTAAACTGGGACCAATGATTAC
CTCATAGGGCTGTTGTGAGGATTAGGATGAA~~AA~~ACTGTGAAAGTGC~~CT~~AGGCAGTGC~~CC~~AGC
CAAATAGGAGGCATTCAATGAACATT~~TT~~GCATATAAA~~CC~~AAAATAACTGTTATCAAT
AAAAACTTGCATCCAACATGAATT~~CC~~AGCCGATGATAATCCAGGCCAAAGGTTAGTTGTT
GTTATT~~CC~~CTGTATTATT~~TT~~CTTCATTACAAAAGAAATGCAAGTTCATTGTAACAATCCA
AACAAACCTCACGATATAAA~~AA~~ATGAAAGTATC~~CT~~C~~CT~~CAAAA

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FIGURE 120

MVAATVAAAWLLLWAAACAAQQEQDFYDFKAVNIRGKLVSLKYRGSVSLVVNVASECGFTDQ
HYRALQQQLQRDLGPHHFNVLAFFCNQFGQQEPDSNKEIESFARRTYSVSFPMFSKIAVTGTG
AHPAFKYLAQTSGKEPTWNFWKYLVAPDGKVVGAWDPTVSVEEVRPQITALVRKLILLKREDL

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FIGURE 121

CGGACGCGTGGCGGGCGGGACGCAGGGCAAAGCGAGCC**ATGG**CTGTCTACGTGGGATGC
TGCCTGGGAGGCTGTGCGCCGGAGCTGGGGTGCTGGGGCCGGCCCTCT
CGGAGTTGGCAGGAAGCCAGGTTGCAGGGTGTCCGCTTCCTCAGTTCCAGAGAGGTGGATCG
CATGGTCTCCACGCCATCGGAGGCCTCAGCTACGTTCAGGGGTGCACCAAAAGCATCTA
ACAGCAAGACTGTGGGCCAGTGCCTGGAGACACAGCACAGAGGGTCCCAGAACGAGAGGCC
TTGGTCGTCTCCATGAAGACGTCAAGGAGGAGGTGGACAA
AGCTGCTTCTGGCCTCTGAGCATTGGCCTCTGCAAAGGTGACCGGCTGGCATGTGGGAC
CTAACTCTATGCATGGGTGCTCATGCAGTTGCCACCGCCAGGGGGCATCATTCTGGT
TCTGTGAACCCAGCCTACCAAGGCTATGAACTGGAGTATGTCCTCAAGAACGGTGGCTGCAA
GGCCCTGTGTTCCCCAAGCAATTCAAGACCCAGCAATACTACAACGTCCTGAAGCAGATCT
GTCCAGAAGTGGAGAATGCCAGCCAGGGGCTTGAAGAGTCAGAGGCTCCAGATCTGACC
ACAGTCATCTCGGTGGATGCCCTTGCAGGGGACCTGCTCTGGATGAAGTGGTGGCGGC
TGGCAGCACCGCAGCATTGGACCAGCTCCAATACAACAGCAGTTCTGTCTGCCATG
ACCCCATCAACATCCAGTTCACCTCGGGACAACAGGCAGCCAAAGGGGCCACCCCTCTCC
CACTACAACATTGTCAACAACCTCAACATTAGGAGAGCCTGAAACTGCATGAGAAC
ACCAAGCAGTTGGATGATCCTGCCAACCCCCGTACCATTCGCTGGTTCCGTGGCAG
GCACAATGATGTGCTGATGTACGGTGCACCCCTCATCCTGGCCTCTCCATTTCAATGGC
AAGAACGGACTGGAGGCCATCAGCAGAGAGAGGGCACCTTCTGTATGGTACCCCCACGAT
GTTCGTGACATTCTGAACCAGCCAGACTTCTCCAGTTATGACATCTGACCATGTGTGGAG
GTGTCATTGCTGGTCCCCCTGCACCTCCAGACTTGTATCCGAGCCATCATCAACAGATAAT
ATGAAGGACCTGGTGGTTGCTTATGAAACCACAGAGAACAGTCCCCTGACATTGCGCAGCT
CCCTGAGGACACTGTGGAGCAGAAGGAGAAAGCGTGGCAGAATTATGCCCTCACACGGAGG
CCCGGATCATGAACATGGAGGCAGGGACGCTGGCAAAGCTGAACACGCCGGGAGCTGTGC
ATCCGAGGGTACTGCGTCATGCTGGCTACTGGGGTGAGCCTCAGAACAGAGAGAAC
GGATCAGGACAAGTGGTATTGGACAGGAGATGTCGCCACAATGAATGAGCAGGGCTCTGCA
AGATCGTGGCCGCTCAAGGATATGATCATCCGGGTGGTGAGAACATCTACCCCGAGAG
CTCGAGGACTTCTTCACACACACCGAAGGTGCAGGAAGTGCAGGTGGTGGAGTGAAGGA
CGATCGGATGGGAAAGAGATTGTGCTGCATTGGCTGAAGGACGGGAGGAGACCACGG
TGGAGGAGATAAAAGCTTCTGCAAAGGAAGATCTCTCACCTCAAGATTCAAACATTGAGA
GTGTTGTACAAACTACCCCTCACCATTCAAGGAAAGATCCAGAAATTCAAACATTGAGA
GCAGATGGAACGACATCTAAATCTG**TGA**ATAAAAGCAGCAGGCCCTGCTGGCCGGTGGCTT
GACTCTCTCTGTGAGAATGCAACCTGGCTTATGCACCTAGATGTCCCCAGCACCCAGTC
TGAGCCAGGCACATCAAATGTCAAGGAATTGACTGAACGAACTAAGAGCTCCTGGATGGTC
CGGGAACTCGCCTGGCACAAGGTGCCAAAGGCAGGCAGCCTGCCAGGCCCTCCCTCG
TCCATCCCCACATTCCCTGTCTGTCCTGTGATTGGCATAAAGAGCTTCTGTTTCTT
GAAAAA

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FIGURE 122

MAVYVGMLRLGRLCAGSSGVLGARAALSRSWQEARNLQGVRFLOSSREVDRMVSTPIGGLSYVQ
GCTKKHLSKTVGQCLETTAQRPVPEREALVVLHEDVRLTFAQLKEEVDKAASGLLSIGLCKG
DRLGMWGPNSYAWVLMQLATAQAGIILVSVNPAYQAMELEYVLKKVGCKALVFPKQFKTQQY
YNVLKQICPEVENAQPGALKSQRLPDLTVISVDAPLPGTLLLDEVVAAGSTRQHLDQLQYN
QQFLSCHDPINIQFTSGTTGSPKGATLSHYNIVNNSNILGERLKLHEKTPEQLRMILPNPLY
HCLGSVAGTMMCLMYGATLILASPIFNGKKALEAISRERGTFLYGTPTMFVDILNQPDFSSY
DISTMCGGVIAGSPAPPELIRAIINKINMKDLVVAYGTTENSPTFAHFPEDTVEQKAESVG
RIMPHTEARIMNMEAGTLAKLNTPGELCIRGYCVMLGYWGEPKTEEAVDQDKWYWTGDVAT
MNEQGFCKIVGRSKDMIIRGGENIYPAELEDFFHTHPKVQEVAQVVGVKDDRMGEEICACIRL
KDGEEETTVEEIKAFCKGKISHFKIPKYIVFVTNYPLTISGKIQKFKLREQMERHLNL

Signal Peptide:

amino acids 1-22

Transmembrane Domains:

amino acids 140-161, 213-229, 312-334

Putative AMP-binding Domain Signature:

amino acids 260-271

N-myristoylation Sites:amino acids 19-24, 22-27, 120-125, 203-208, 268-273, 272-277,
314-319, 318-323, 379-384, 380-385, 409-413**N-glycosylation Site:**

amino acids 282-285

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FIGURE 123

CAACTCCAACATTTAGGAGAGCGCCTGAAACTGCATGAGAAGACACCAGAGCAGTTGCGGA
TGATCCTGCCAACCCCTGTACCATTGCCCTGGGTTCCGTGGCAGGCACAATGATGTGTCTG
ATGTACGGTGCCACCCTCATCCTGGCCTCTCCATCTTCAATGGCAAGAAGGCACTGGAGGC
CATCAGCAGAGAGAGAGGGCACCTCCTGTATGGTACCCCCACGATGTTGGACATTCTGA
ACCAGCCAGACTTCTCCAGTTATGACATCTGACCATGTGTGGAGGTGTCATTGCTGGGTCC
CCTGCACCTCCAGAGTTGATCCGAGCCATCATCAACAAGATAAATATGAAGGACCTGGTGGT
TGCTTATGGAACCACAGAGAACAGTCCCGTGACATTGCGCACTTCCCTGAGGACACTGTGG
AGCAGAAGGCAGAAAGCGTGGGCAGAATTATGCCCTCACACGGAGGCGCGGATCATGAACATG
GAGGCAGGGACGCTGGCAAAGCTGAACACGCCCGGGAGCTGTGCATCCGAGGGTACTGCGT
CATGCTGGCTACTGGGTGAGCCTCAGAAGACAGAGGAAGCAGTGGATCAGGACAAGTGGT
ATTGGACAGGAGATGTCGCCAC

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FIGURE 124

GAGCAGGACGGAGCCATGGACCCGCCAGGAAAGCAGGTGCCAGGCCATGATCTGGACTGC
AGGCTGGCTGCTGCTGCTGCTGCTCGCCGGAGGAGCGCAGGCCCTGGAGTGCTACAGCTGCG
TGCAGAAAGCAGATGACGGATGCTCCCCAACAGATGAAGACAGTGAAGTGCAGCGCCGGC
GTGGACGTCTGCACCGAGGCCGTGGGGCGGTGGAGACCATCCACGGACAATTCTCGCTGGC
AGTGCAGGGTTGCGGTTGGACTCCCCGGCAAGAACGACGGATCGCTGCAACGCCAGCTAACCTC
TTCTGGCGTTCATCCAGCTGCAGCAATGCGCTCAGGATCGCTGCAACGCCAGCTAACCTC
ACCTCGCGGCCGCTCGACCCGGCAGGTAATGAGAGTCATAACCGCCAACGGCGTGGAGTG
CTACAGCTGTGTGGCCTGAGCCGGAGGCCTGCCAGGGTACATGCCGCCGGTCGTGAGCT
GCTACAACGCCAGCGATCATGTCATAAGGGCTGCTCGACGGCAACGTCACCTGACGGCA
GCTAATGTGACTGTGTCCTTGCCCTGTCGGGGCTGTGTCCAGGATGAATTCTGCACTCGGGA
TGGAGTAACAGGCCAGGGTTACGCTCAGTGGCTCCTGTTGCCAGGGTCCGGCTGTAACCT
CTGACCTCCGCAACAAGACCTACTTCTCCCTCGAATCCCACCCCTGTCCGGCTGCCCT
CCAGAGCCCACGACTGTGGCCTCAACCACATCTGTCAACCACCTACCTCGGCCCCAGTGAG
ACCCACATCCACCAACCAAAACCATGCCAGCGCAACCAGTCAGACTCCGAGACAGGGAGTAG
AACACGAGGCCTCCGGATGAGGAGCCAGGTTGACTGGAGGCCGCGCTGGCCACCAGGAC
CGCAGCAATTCAAGGGAGTATCCTGCAAAAGGGGGCCCCAGCAGCCCCATAATAAGGCTG
TGTGGCTCCACAGCTGGATTGGCAGCCCTCTGTTGCCGTGGCTGCTGGTGTCCCTACTGT
GAGCTTCTCCACCTGAAATTCCCTCTCACCTACTTCTCTGGCCCTGGTACCCCTTTCT
CATCACTTCTGTTCCCACCACTGGACTGGCTGGCCAGCCCTGTTTCCAACATTCCC
CAGTATCCCCAGCTCTGCTGCGCTGGTTGCCGCTTGGAAATAAAACCGTTGTATAT
ATTCTGCCAGGGGTGTTCTAGCTTTGAGGACAGCTCCTGTATCCTCTCATCCTGTCTC
TCCGCTGTCTCTGTGATGTTAGGACAGAGTGAGAGAAGTCAGCTGTCACGGGAAGGTG
AGAGAGAGGATGCTAAGCTCCTACTCACTTCTCTAGCCAGCCTGGACTTGGAGCGTGG
GGTGGGTGGGACAATGGCTCCCCACTCTAACGCACTGCCTCCCTACTCCCCGATCTTGGG
GAATCGGTTCCCCATATGTCTCCTTACTAGACTGTGAGCTCTCGAGGGGGGGCCGGTAC
CCAATTGCCCTATAGTGAGTCGTA

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FIGURE 125

MDPARKAGAQAMIWTAGWLLLLLRRGAQALECYSCVQKADDGSPNKMKTVKCAPGVDVCT
EAVGAVETIHGQFSLAVRGCGSGLPGKNDRGLDLHGLLAFIQLQQCAQDRCNAKLNLTSRAL
DPAGNESAYPPNGVECYSCVGLSREACQGTSPPVSCYNASDHVYKGCFDGNVTLTAANVT
SLPVRCVQDEFCTRDTGVTGPGFTLSGSCCQGSRCNSDLRNKTYFSPRIPLVRLPPPEPTT
VASTTSVTTSTSAPVRPTSTTKPMPAPTSQTPRQGVEHEASRDEEPRLTGGAAGHQDRSNSG
QYPAKGGPQQPHNKGCVAPTAGLAALLLAVAAGVLL

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FIGURE 126

CGGGACTCGGCAGGGCCTCCTGGGAGTCTCGGAGGGGACCGGCTGTGCAGACGCCATGGAGT
TGGTCTGGTCTTCCTCTGCAGCCTGCTGGCCCCATGGTCTGCCAGTGCAGCTGAAAAG
GAGAAGGAAATGGACCCCTTCATTATGATTACAGACCCCTGAGGATTGGGGACTGGTGT
CGCTGTGGTCTCTCGGTTGGATCCTCTTATCCTAAGTCGCAGGTGCAAGTGCAGTT
TCAATCAGAACAGCCCCGGGCCCCAGGAGATGAGGAAGCCCAGGTGGAGAACCTCATCACC
AATGCAACAGAGCCCCAGAACGAGAGAACTGAAGTGCAGCCATCAGTGGAAAGCCTCTGGAA
CCTGAGGCAGGCTGCTGAACCTTGGATGCAAATGTCGATGCTTAAGAAAACCGGCCACTTC
AGCAACAGCCCTTCCCCAGGAGAACCCAAGAACCTGTGTCCCCACCCATCCCCCTCTA
ACACCATTCCCTCACCTGATGATGCAACTAACACTTGCCTCCCCACTGCAGCCTGCGTCCT
GCCCACCTCCCGTGTGTGTGTGTGTGTGTGTACTGTGTGTGTTGCTAACTGTG
GTCTTGTGGCTACTTGTGGATGGTATTGTGTTGTTAGTGAACGTGGACTCGCTT
CCCAGGCAGGGCTGAGCCACATGGCATCTGCTCCTCCCTGCCCCCGTGGCCCTCCATCAC
CTTCTGCTCCTAGGAGGCTGCTTGTGCCCAGAACAGCCCCCTCCCTGATTTAGGGATGC
GTAGGGTAAGAGCACGGCAGTGGCTTCAGTCGTTGGACCTGGGAAGGTTGAGCAC
TTTGTCACTCATTCTCATGGACTCCTTCACTCCTTAACAAAACCTGCTCCTTATCCC
ACCTGATCCCAGTCTGAAGGTCTTAGCAACTGGAGATACAAAGCAAGGAGCTGGTGA
CAGCGTTGACGTCAGGCAGGCTATGCCCTCCGTGGTAATTCTCCAGGGCTTCCACG
AGGAGTCCCCATCTGCCCCGCCCTTCACAGAGCGCCGGGATTCCAGGCCAGGGCTT
ACTCTGCCCTGGGAATGTGTCCCTGCATATCTCTCAGCAATAACTCCATGGCTCTGG
GACCCCTACCCCTCCAACCTTCCCTGCTCTGAGACTCAATCTACAGCCCAGCTCATCCAG
ATGCAGACTACAGTCCCTGCAATTGGGTCTCTGGCAGGCAATAGTTGAAGGACTCCTGTT
GTTGGGCCAGCACACCGGGATGGATGGAGGGAGAGCAGAGGCCTTGCTCTGCCTACG
TCCCTTAGATGGCAGCAGAGGCAACTCCCGCATCCTTGTCTGCCTGCGGTGGTCAGA
GCGGTGAGCGAGGTGGTTGGAGACTCAGCAGGCTCCGTGCAGCCCTGGGAACAGTGAGAG
GTTGAAGGTATAACGAGAGTGGAACTCAACCCAGATCCGCCCTCCTGCTCTGTGTT
CCCGCGAAACCAACCAACCGTGCCTGTGACCCATTGCTGTTCTGTATCGTATCT
CCTCAACAACAACAGAAAAAGGAATAAAATCCTTGTTCCT

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FIGURE 127

MELVLVFLCSLLAPMVLASAAEKEKEMDPFHODYQTLRIGGLVFAVVLFSVGILLILSRRCK
CSFNQKPRAPGDEEAQVENLITANATEPQKQRTEVQPSGGSLWNLRRILLEPLDANVDA

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FIGURE 128

AAACTTGACGCCATGAAAGATCCGGTCCTCCTGCCGTGGTGCCTCCTCCCTGGTGCT
CCACTCTGCCAGGGAGCCACCCCTGGTGGCCTGAGGAAGAAAGCACCATTGAGAATTATG
CGTCACGACCCGAGGCCTTAACACCCCGTTGAACATCGACAAATTGCGATCTCGCTT
AAGGCTGATGAGTTCTGAACCTGGCACGCCCTTTGAGTCATCAAAGGAAACTTCCTT
CCTCAACTGGGATGCCCTTCCTAACGCTGAAAGGACTGAGGAGCGCAACTCCTGATGCCAGT
GACCATGACCTCCACTGGAAGAGGGGGCTAGCGTGAGCGCTGATTCTCAACCTACCATAACT
CTTCCTGCCTCAGGAACTCCAATAAACATTTCCATCCAAA

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FIGURE 129

MKIPVLPAVVLLSLLVLHSAQGATLGGPEEESTIENYASRPEAFNTPFLNIDKLRSAFKADEFLNWHALFESIKRKLPFLNWDAFPKLKGLRSATPDAQ

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FIGURE 130

CAGTTCTGAAATCAATGGAGTTAATTAGGAAATACAAACCAGCCATGGGGTGGAGATTGC
CTTGCCCTCAGTGATTCTCACCTGCCTCTCCCTCTGGCAGCAGGAGTCTCCCAGGTTGTT
TTCTCCAGCCAGTTCCAACTCAGGAGACAGGTCCCAAGGCCATGGGAGATCTCTCCTGTGGC
TTGCCGGCCACTCATGAGAGTGTGTTGTGAAAGTATTTTAAAGTACTGTTGACTTCT
TCATGATTTAATAACCATCCTTGCAGTTTATGAGGCTTAGGGGAATGTCAACCCCTCA
AATTTTGTATAGATGGCTTCCATTACCCACCACTATTTAAGGTCCCTTATTTT
AGGTTCAAGGTTCAATTGACTTGAGAAAGTGCCTCTGCAGCTCATTGATTTGTTATC
TTCACATTAAATTGTAACGATTAAGAATAAGAGCACGCAGACCTCTAGGAGAATATT
TATCCCTGGGTGCCCTGACACATTATGTAGTGATCCCACAAATGTGATTGTTAATTAAA
TGTTATTCTAATATTAGTACATTCAAGTTGTGATGTAATATGAATAACCAGAATCTATTCTT
AAAAGTTTGAGTATTTTCAACTAGATATTGATAGAAAGACTGAATAGTGATG

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FIGURE 131

MGVEIAFASVILTCLSLLAAGVSQVVLLQPVPTQETGPKAMGDLSCGFAGHS

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FIGURE 132

GGGGAATCTGCAGTAGGTCTGCCGGCGATGGAGTGGTGGGCTAGCTGCCGCTCGGCTCTG
GCTGCTGTTGTCCTCCTGCCCTCAGCGCAGGGCCGCCAGAAGGAGTCAGGTTCAAATGGA
AAGTATTATTGACCAAATTAAACAGGTCTTGGAGAATTACGAACCATGTTCAAGTCAAAAC
TGCAGCTGCTACCATGGTGTAGAGAGGATCTAACTCCCTCGAGGAGGCATCTCCAG
GAAGATGATGGCAGAGGTAGTCAGACGGAAGCTAGGGACCCACTATCAGATCACTAAGAAC
GACTGTACCGGGAAAATGACTGCATGTTCCCTCAAGGTGTAGTGGTGTGAGCACTTATT
TTGGAAGTGATCGGGCGTCTCCCTGACATGGAGATGGTGTCAATGTACGAGATTATCCTCA
GGTTCCCTAAATGGATGGAGCCTGCCATCCCAGTCTCCTCAGTAAGACATCAGAGTACC
ATGATATCATGTATCCTGCTGGACATTGGAAAGGGGACCTGCTGTTGGCCAATTAT
CCTACAGGTCTGGACGGTGGACCTCTCAGAGAAGATCTGGTAAGGTAGCAGCACAGTG
GCCATGGAAAAAGAAAAACTCTACAGCATATTCCGAGGATCAAGGACAAGTCCAGAACGAG
ATCCTCTCATTCTTCTGTCTCGGAAAAACCCAAAACCTTGTGATGCAGAATACACCAAAAC
CAGGCCTGGAAATCTATGAAAGATACTTAGGAAAGCCAGCTGCTAAGGATGTCCATTTGT
GGATCACTGCAAATACAAGTATCTGTTAATTTCGAGGCGTAGCTGCAAGTTCGGTTTA
AACACCTCTCCTGTGTGGCTACTGTTCCATGTTGGTGTGAGTGGCTAGAATTCTC
TATCCACAGCTGAAGCCATGGGTTCACTATATCCCAGTCAAAACAGATCTCTCCAATGTCCA
AGAGCTGTTACAATTGTAAAAGCAAATGATGATGAGCTCAAGAGATTGCTGAAAGGGAA
GCCAGTTATTAGGAACCATTGCAAGATGGATGACATCACCTGTTACTGGGAGAACCTTTG
AGTGAATACTCTAAATTCTGTCTTATAATGTAACGAGAAGGAAAGGTTATGATCAAATTAT
TCCCAAAATGTTGAAAACGTAACTTAGTAGTCATCATAGGACCATAGCCTCTTGTGGCA
ACAGATCTCAGATATCCTACGGTGAGAAGCTTACCATAGCTGGCTCCTACCTGAATA
TCTGCTATCAAGCCAAATACCTGGTTTCCATTATGCTGCAACCCAGAGCAACTCTTGAGA
AAGATTAAAATGTGCTAATACACTGATGAGCTCAACCTTGGATGAAATAAGGA
CCAGAAATCGTGAGATGTGGATTGAAACCCAACTCTACCTTCATTCTTAAGACCAATC
ACAGCTTGTGCCTCAGATCATCCACCTGTGTGAGTCCATCACTGTGAAATTGACTGTCCA
TGTGATGATGCCCTTGTCCCATTATTGGAGCAGAAAATTGTCATTGGAAAGTAGTACAA
CTCATTGCTGGAATTGTGAAATTATTCAAGGCAGTCTGTCACATTATTTAATGTAGG
AAACCCCTATGGGTTATGAAAATACTTGGGATCATTCTCTGAATGGCTAAGGAAGCGG
TAGCCATGCCATGCAATGATGAGTGTAGGAGTTCTCTTGTAAAACCATAAAACTCTGTTACTCAG
GAGGTTCTATAATGCCACATAGAAAGAGGCCAATTGCATGAGTAATTATTGCAATTGGATT
TCAGGTTCCCTTTGTGCCTCATGCCCTACTTCTTAATGCCCTCTAAAGCCAAA

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FIGURE 133

MEWWASSPLRLWLLLFLLPQAQGRQKESGSKWKVFIDQINRSLENYEPCSSQNCSCYHGVIE
EDLTPFRGGISRKMMAEVVRRKLGTHYQITKNRLYRENDCMFPSRCSGVEHFILEVIGRLPD
MEMVINVRDYPQVPKWMEPAIPVFSFSKTSEYHDIMYPAWTFWEGGPAAVWPIYPTGLGRWDL
FREDLVRSAAQWPWKKKNSTAYFRGSRTSPERDPLILLSRKNPKLVDAEYTKNQAWKSMKDT
LGKPAAKDVHLVDHCKYKYLNFNFRGVAASFRFKHLFLCGSLVFHVGDEWLEFFYPQLKPWVH
YIPVKT,DLSNVQELLQFVKANDDVAQEIAERGSQFIRNHLQMDDITCYWENLLSEYSKFLSY
NVTRRKGYDQIIPKMLKTEL

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FIGURE 134

CACCCCTCCATTCTCGCCATGGCCCTGCACTGCTCCTGATCCCTGCTGCCCTGCCCTCTT
TCATCCTGGCCTTGGCACCGGAGTGGAGTTCGTGCCTTACCTCCCTCGGCCACTTCTT
GGAGGGATCCCGGAGTCTGGTGGTCCGGATGCCGCCAGGGATGGCTGGCTGCCCTGCAGGA
CCGCAGCATCCTGCCCTGGCATGGATCTGGGCTCCTGCTTCTATTGTGGCAGC
ACAGCCTCATGGCAGCTGAAAGAGTGAAGGCATGGACATCCGGTACTTGGGTCCCTCAG
AGGTCACTGTATGTGGCCTGCACTGCCCTGGCCTGCAGCTGGTATGCGGTACTGGGAGCC
CATACCAAAGGCCCTGTGTTGGGAGGCTGGGCTGAGCCATGGGCCACCTGGTGCCGC
TCCTCTGCTTGTGCTCCATGTCACTCCTGGCTCCTCATCTTAGCATCCTCTCGTCTT
GACTATGCTGAGCTCATGGCCTCAAACAGGTATACTACCATGTGCTGGGCTGGCGAGCC
TCTGGCCTGAAGTCTCCCGGGCTCTCAGACTCTCTCCACCTGCCACCCAGTGTG
TGGAGCTGCTGACAGTGCTGTGGTGGCCTACCCCTGGCACGGACCGTCTCCCTTGCT
TTCCTCCTTACCTCTACCTGGCCTGGCTCACGGCTTGATCAGCAAGACCTCCGCTACCT
CCGGGCCAGCTACAAAGAAAACCTCACCTGCTCTCGGCCAGGATGGGAGGCAGAGT
GAGGAGCTCACTCTGGTTACAAGCCCTGTTCTCCCTCCCAC**TA****GAATTCTAAATCCTAAC**
ATCCAGGCCCTGGCTGCTTCATGCCAGAGGCCAAATCCATGGACTGAAGGAGATGCCCTT
CTACTACTTGAGACTTTATTCTCTGGTCCAGCTCCATACCTAAATTCTGAGTTCAGCCA
CTGAACCTCAAGGTCCACTTCTCACCAAGCAAGGAAGAGTGGGTATGGAAGTCATCTGTCCC
TTCACTGTTAGAGCATGACACTCTCCCCCTCAACAGCCTCTGAGAAGGAAGGATCTGCC
CTGACCACTCCCTGGCACTGTTACTTGCTCTGCCTCAGGGTCCCTGCACCGCT
GGCTTCCACTCCAAGAAGGTGGACCAGGGTCTGCAAGTTCAACGGTCATAGCTGCCCTCCA
GGCCCCAACCTTGCCTCACCACTCCGCCCTAGTCTCTGCACCTCCTAGGCCCTGCCT
GGGCTCAGACCCCAACCTAGTCAAGGGATTCTCCTGCTCTAACTCGATGACTGGGCTC
CCTGCTCTCCGAGGAAGATGCTCTGCAGGAAAATAAAAGTCAGCCTTTCTAAAAAAA

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FIGURE 135

MAPALLIPIAALASFILAFTGTGVEFVRFTSLRPLLGGIPESGGPDARQGWLAALQDRSILAP
LAWDLGLLLLFGQHSLMAAERVKAWSRYFGVLQRSLYVACTALALQLVMRYWEPIPKGPV
LWEARAEPWATWVPLLFCFVLHVISWLLIFSILLVFDYAEMLGKQVYYHVLGLGEPLALKSP
RALRLFSHLRHPVCVELLTVLWVVPTLGTDRLLAFLLTLYLGLAHGLDQQDLRYLRAQLQR
KLHLLSRPQDGAE

Signal sequence:

amino acids 1-13

Transmembrane domains:

amino acids 58-76, 99-113, 141-159, 203-222

N-myristoylation sites:

amino acids 37-43, 42-48, 229-235

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FIGURE 136

CCGAGCACAGGAGATTGCCTGCCTTAGGAGGTGGCTGCCTGTGGAAAAGCTATCAAGGA
AGAAAATTGCCAACCATGTCTTTCTGTTTCAGAGTAGTTACAACAGATCTGAGTGT
TTAATTAAAGCATGGAATACAGAAAACAACAAAAACTTAAGCTTAATTCATCTGGAATT
CCACAGTTCTTAGCTCCCTGGACCCGGTTGACCTGTTGGCTCTCCCGCTGGCTGCTCTA
TCACGTGGTGCCTCCGACTACTCACCCCCGAGTGTAAAGAACCTTCGGCTCGCGTGCCTCTG
AGCTGCTGTGGATGGCCTCGGCTCTGGACTGTCCTCCGAGTAGGATGTCAGTGAGATCC
CTCAAATGGAGCCTCGTGTGTCACTCCTGAGTTCTTGTGATGTGGTACCTCAGCCT
TCCCCACTACAATGTGATAGAACCGGTAACTGGATGACTCTATGAGTATGAGCCGATT
ACAGACAAGACTTCACTCACACTCGAGAGCATTCAAACGTCTCATCAAATCCATT
CTGGTCATTCTGGTGACCTCCACCCCTCAGATGTGAAAGCCAGGCAGGCCATTAGAGTTAC
TTGGGGTGAAGAAAAGTCTGGTGGGATATGAGGTTCTTACATTTCTTATTAGGCCAAG
AGGCTGAAAGGAAGACAAAATGTTGGCATTGTCCTTAGAGGATGAACACCTTCTTATGGT
GACATAATCCGACAAGATTTTAGACACATATAAACCTGACCTTGAAAACCATTATGGC
ATTCAAGGTGGTAACTGAGTTGCCAAGTACGTAACTGAGACAGACACTGATG
TTTCATCAATACTGGCAATTAGTGAAGTATCTTAAACCTAAACCACTCAGAGAAGTT
TTCACAGGTATCCTCTAATTGATAATTATTCTATAGAGGATTTACCAAAAAACCCATAT
TTCTTACCCAGGAGTATCCTTCAAGGTGGTCCACTGCACTGGGTTGGGTTATATAA
TGTCCAGAGATTTGGTGCCAAGGATCTATGAAATGATGGTCACGTAAAACCCATCAAGTT
GAAGATGTTATGTCGGATCTGTTGAATTATTAAAAGTGAACATTCAATTCCAGAAGA
CACAAATCTTCTTCTATATAGAATCCATTGGATGTCGACTGAGACGTGATTG
CAGCCCATGGCTTCTTCCAAGGAGATCATCACTTTGGCAGGTATGCTAAGGAACACC
ACATGCCATTATTCACATTCTACAAAAGCCTAGAAGGACAGGATACCTGTGGAAA
GTGTTAAATAAGTAGGTACTGTGGAAAATTCACTGGGAGGTCACTGTGCTGGCTTACACTG
AACTGAAACTCATGAAAACCCAGACTGGAGACTGGAGGGTACACTTGTGATTATTAGTC
AGGCCCTCAAAGATGATATGTGGAGGAATTAAATATAAGGAATTGGAGGTTTGCTAAA
GAAATTAAATAGGACAAACAATTGGACATGTCATTGTAAGTCAACTGAGTAAAGGG
TGTTACTGAGTTATAAGCTCACTAGGCTGAAAAACAAAACAATGTAGAGTTATTGATTG
AACAAATGTAGTCACTTGAAGGTTGTATATCTTATGTGGATTACCAATTAAAAATATA
TGTAGTTCTGTGTCAAAAACTCTTCACTGAAGTTACTGAAGTTACAACAAAATTACCTGTTT
TGGTCATTATAAAAGTACTTCAAGATGTTGCACTGAGTTACAGTTATTATTAAATTA
CTTCAACTTGTGTTAAATGTTGACGATTCAATACAAGATAAAAAGGATAGTGAAT
CATTCTTACATGCAAACATTCCAGTTACTTAACGATGATCAGTTATTATTGATACATCAC
TCCATTAAATGTAAAGTCATAGGTCAATTGCAATCAGTAATCTCTGGACTTGTTAAAT
ATTTTACTGTGGTAATATAGAGAAGAATTAAAGCAAGAAAATCTGAAAA

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FIGURE 137

MASALWTVLPSRMSLRSLKWSLLLLSLLSFFVMWYLSLPHYNVIERVNWMYFYEYEPIYRQD
FHFTLREHSNC SHQN PFLVILVTSHPSDVKARQAIRVTWGEKKSWWGYEVLTFFLLGQEAEK
EDKMLALSLEDEHLLYGDII RQDFLDTNNLTLKTI MAFRWVTEFCPNAKYVMKTDTDVFIN
TGNLVKYLLNLNHSEKFFTGYPLIDNYSYRGFYQKTHISYQEYPFKVFPPYCSGLGYIMSRD
LVPRIYEMMGHVKPIKFEDVYVGICLNLLKVNIHIPEDTNLFFLYRIHLDVCQLRRVIAAHG
FSSKEIITFWQVMLRNTTCHY

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FIGURE 138

CCTCTGTCCACTGCTTCGTGAAGACAAGATGAAGTTACAATTGTCTTGCTGGACTTCTT
GGAGTCTTCTAGCTCCTGCCCTAGCTAACTATAATATCAACGTCAATGATGACAACAACAA
TGCTGGAAGTGGGCAGCAGTCAGTGAGTGTCAACAATGAACACAATGTGGCCAATGTTGACA
ATAACAACGGATGGGACTCCTGGAATTCCATCTGGGATTATGGAAATGGCTTGCTGCAACC
AGACTCTTCAAAAGAAGACATGCATTGTGCACAAAATGAACAAGGAAGTCATGCCCTCCAT
TCAATCCCTGATGCACTGGTCAAGGAAAAGAAGCTTCAGGTAAGGGACCAGGAGGACCAC
CTCCCAAGGGCCTGATGTACTCAGTCAACCCAAACAAAGTCGATGACCTGAGCAAGTCGGA
AAAAACATTGCAAACATGTGCGTGGATTCCAACATACATGGCTGAGGAGATGCAAGAGGC
AAGCCTGTTTTTACTCAGGAACCGTGGAGAACTAAACAATTAAAGCCACTATGGATTGAGCATT
CCTCTGTGGAGACACGGTGGAGAACTAAACAATTAAAGCCACTATGGATTGAGCATT
CTGAATATGCTGTGCAGAAAAAATATGGGCTCCAGTGGTTTACCATGTCATTCTGAAATT
TTTCTCTACTAGTTATGTTGATTCTTAAGTTCAATAAAATCATTAGCATTGAAAAAAA

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FIGURE 139

MKFTIVFAGLLGVFLAPALANYNINVNDNNNAGSGQQSVVNNEHNVANVDNNNGWDSWNS
IWDYNGNGFAATRLFQKKTCIVHKMNKEVMPSIQSILDALVKEKKLQGKPGGPPPGLMYSVN
PNKVDDLSKFGKNIANMCRGIPTYMAEEMQEASLFFYSGTCYTTSVLWIVDISFCGDTVEN

Signal Peptide:

amino acids 1-20

N-myristoylation Sites:

amino acids 67-72, 118-123, 163-168

Flavodoxin protein homology:

amino acids 156-174

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FIGURE 140

CATTTCTGAAACTAATCGTGTAGAATTGACTTGAAAGCATTGCTTTACAGAAGTATA
TTAACCTTTAGGAGTAATTCAGTTGGATTGTAATATGAAATAATTAAAAGGGCTTCG
CTCATATATAGGAAATCGCATATGGCCTAGTATTAAATTCTTATTGCTTACTGATTTTT
TGAGTTAAGAGTTGTTATATGCTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAAA
GAATAAAGTAGATTGAGTCTCCAATTTATGTAAGCTTCAGAAGAACTGGTTGTTACATG
CAAGCTTATAGTTGAAATATTTTCAAGGAATTACATGAATGACAGTCTCGAACCAATGTGT
TTGTTCGATTCACCAGAGACTATAGCATGTGCTGCATCTACCTGCAGCTAGAGCACTT
CAGATTCCGTTGCCAACTCGTCCCCATTGGTTCTCTTTGGTACTACAGAAGAGGAAAT
CCAGGAAATCTGCATAGAAACACTTAGGTTATACCAGAAAAAGCCAAACTATGAATTAC
TGGAAAAAGAAGTAGAAAAAGAAAAGTAGCCTTACAAGAAGCCAAATTAAAGCAAAGGGAA
TTGAATCCGGATGGAACTCCAGCCCTTCAACCCTGGGTGGATTTCTCCAGCCTCCAAGCC
ATCATCACCAAGAGAAGTAAAAGCTGAAGAGAAATCCAATCTCATTAAATGTGAAGACAG
TCAAAAAAGAACCTGAGGATAGACAACAGGCTTCAAAAGCCCTACAATGGTGTAAAGAAAA
GACAGCAAGAGAAGTAGAAATAGCAGAAGTGCAGTCAGTGAAAGCCTTACAATGGTGTAAAGAAAA
TTCTAGATCACATACTCCAAGAAGACACTATAATAATAGGCGGAGTCGATCTGGAACATACA
GCTCGAGATCAAGAAGCAGGTCCCGCAGTCACAGTGAAAGCCTCGAAGACATCATATCAT
GGTTCTCCTCACCTTAAGGCCAAGCATAACCAGAGATGATTAAAAAGTTCAAACAGACATGG
TCATAAAAGGAAAAATCTGTTCTCGATCTCAGAGCAAGTCTCGGGACTACTCAGATGCAG
CCAAGAAACACAGGCATGAAAGGGACATCATAGGGACAGGCGTGAACGATCTCGCTCTT
GAGAGGTCCCATAAAGCAAGCACCAGGTGGCAGTCGCTCAGGACATGGCAGGCACAGGCG
CTGACTTCTCTCCTTGAGCCTGCATCAGTTGGTTGCCTATCTACAGTGTGATGT
ATGGACTCAATCAAAACATTAAACGCAAACGTGATTAGGATTGATTCTGAAACCTCTA
GGTCTCTAGAACACTGAGGACAGTTCTTGAAAAGAACTATGTTAAATTGGCACATT
AAAATGCCCTAGCAGTATCTAATTAAAACCAGGTCAATTGTACTTTATTAGT
TGTGTATTGTTATTGCTATAAGAACTGGAGCGTGAATTCTGAAAAATGTATCTTATT
ATACAGATAAAATTGCAAGACACTGTTCTATTAAAGTGGTTATTGTTAAATGATGGTGAAT
ACTTTCTTAACACTGGTTGTCTGCATGTGTAAAGATTTCACAAGGAAATAAAACAAAT
CTGTTTTCTAAAAAAAGT

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FIGURE 141

MNDSLRTNVFVRFQPETIACACIYLAARALQIPLPTRPHWFLFGTTEEEIQEICIETRLY
TRKKPNYELLEKEVEKRKVALQEAKLKAKGLNPDGTPALSTLGGFSPASKPSSPREVKAEEK
SPISINVKTVKKEPEDRQQASKSPYNGVRKDSKRSRNSRSASRSRSRTRSRSRSHTPRRHYN
NRRSRSGTYSSRSRSRSRSHSESPRRHHNHGSPHLKAKHTRDDLKSSNRHGHKRKKRSRSQ
SKSRDHSDAAKKHRHERGHHRDRRERSRSFERSHKSKHHGGSRSGHGRHRR

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FIGURE 142

TGGGGATAAAGGAAAAATGGTCAGGTATTAATGGCTTAAAGATTATTGGAAGGGGTTATCA
TTTTTGAANNTATCGGGTCANAATTGNCTTAAAAGCATTGCTTTTACAGAAATATAT
TANCTTTAGAGTAATTCTAGTTGGATTGTAATATGAAATTATTAAAAGGGCTTCGCT
CATATATAGGAAAATCGCATATGGCCTAGTATTAAATTNTTATTGCTTACTGATTTTG
AGTTAAGAGTTGTTATATGNTAGAATATGAGGATGTGAATATAAATAAGAGAAGAAAAAAGA
ATAAAAGTAGATTGAGTCTCCAATTTATGTAAGCTTCAGAAGAACTGGTTGTTACATGCA
AGCTTATAGTTGAAATATTTCAAGGAATTACATGAATGACAGTCTCGAACCAATGTGTT
GTTCGATTCACCAGAGANTATAGCATGTGCTTGCATCTACCTTGCAAGNTAGACACTTCA
GATTCGTTGCCAACTNGTCCCATTGGTTCTTCTTTGGTACTACAGAAGAGGAAATCC
AGGAAATNTGCATAGAAACACTTAGGCTTATACCAGAAAAAGCCAAACTATGAATTACTG
GAAAAAGAAGTAGAAAAAGAAAAGTAGCCTTACAAGAACGCAATTAAAAGCAAAGGGATT
GAATCCGGATGGAACTCCAGCCCTTCAACCCTGGGTGGATTTCTCC

FIGURE 143

GGCACGAGGCCTCGCCAAGCTGGCACGAGGGTGCACCGCGTTCTCGCACCGCTC**ATGGC**
GGTCCTCGGAGTACAGCTGGTGGTACCCCTGCTCACTGCCACCCCATGCACAGGCTGGCGC
CACACTGCTCTCGCGCGCTGGCTGCTCTGTAACGGCAGTTGTTCCGATAAAGCACCCG
TCTGAGGAGGAGCTCGGGCCCTGGCGGGGAAGCCGAGGCCAGAGGCAGGAAAGAGCGGTG
GGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCCCCGAGATGCCCCGTTCCAGCTGG
AGACCTGCCCCCTCACGACCGTGGATGCCCTGGCTCTGCGCTTCTCCTGGAGTACCAAGTGG
TTTGTGGA**CTTGCTGT**TACTCGGGCGCGTGTACCTCTCACAGAGGCCTACTACTACAT
GCTGGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGTGCCTGCTCACGGTACCTTCT
CCATCAAGATGTTCCCTGACAGTGACACGGCTGTACTTCAGGCCGAGGAGGGGGTGAGCGC
TCTGTCTGCCCTCACCTTGCCTTCCTCTTGCCTGCTGGCCATGCTGGTGCAAGTGGTGC
GGAGGAGACCCCTCGAGCTGGGCTGGAGCCTGGCTGGCCAGCATGACCCAGAACTTAGAGC
CACTTCTGAAGAACGAGCAGGGCTGGGACTGGCGCTTCCGTGGCCAAGCTGGCTATCCGCGT
GGACTGGCAGTGGTGGGCTCTGTGCTGGGTGCCTTCCACCTTCCAGGCCTGGCTGG
CCAGACCCACCAGGGACGCACTGACCATGTCGGAGGACAGACCCATGCTGCAGTCCCTCCTGC
ACACCAAGCTTCTGTCTCCCTGTTCATCCTGTGGCTCTGGACAAAGCCCATTGCACGGGAC
TTCCCTGCACCAGCCGCCGTTGGGAGACCGGTTCTCCCTGCTGTCCGATTCTGCCCTCGA
CTCTGGGCCCTCTGGTGCTGGTGGTGCCTGCTGCCGCTGGCGGTGACCCGGCCCC
ACCTGCAGGCCTACCTGTGCCTGGCCAAGGCCCGGGTGGAGCAGCTGCGAAGGGAGGCTGG
CGCATCGAAGCCCCTGAAATCCAGCAGAGGGTGGTCCGAGTCTACTGCTATGTGACCGTGGT
GAGCTTGAGTACCTGACGCCGCTCATCCTCACCCCTCAACTGCAACTTCTGCTCAAGACGC
TGGGAGGCTATTCTGGGCCCTGGGCCAGCTCCTACTATCCCCGACCCATCCTCAGCC
AGCGCTGCCCTCTGGCTCTGGGAGGACGAAGTCCAGCAGACTGCAGCGCGATTGCCGG
GCCCTGGGTGGCCTGCTTACTCCCTCTTCCGTGGCGCTGGCCTACCTCATCTGGT
GGACGGCTGCCAGCTGCTGCCAGCCTTTGGCCTACTTCCACCAGCACTGGCA
GGCTCC**TAG**CTGCCTGCAGACCCCTCTGGGCCCTGAGGTCTGTTCTGGGCAGCGGGACA
CTAGCCTGCCCTCTGTTGCCCTGGGCCAGCTGCAAGGTGGGCCGGACTCCCC
GGCGTTCCCTCACCAAGTGCCTGACCCGCCCTGGACGCCAGTTCTGCTCA
GAACCTGTCTCTCCCTGGGCCAGCAGCATGAGGGTCCCAGGCCATTGTCTCCGAAGCGTATG
TGCCAGGTTGAGTGGCGAGGGTGATGCTGGCTGCTTCTGAACAAATAAGGAGCATGCC
GATTTTAA

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FIGURE 144

MAVLGVQLVVTLLTATLMHRLAPHCSFARWLLCNGSLFRYKHPSEEELRALAGKPRPRGRKE
RWANGLSEEKPLSVPRDAPFQLETCPLTTVDALVLRFFLEYQWFVDFAVYSGGVYLFTTEAYY
YMLGPAKETNIAVFWCLLTVTFSIKMFLTVTRLYFSAEEGERSVCLTFAFLFLLLAMLVQV
VREETLELGLEPGLASMTQNLEPLLKKQGWDWALPVAKLAIRVGLAVVGSVLGAFLTFPGLR
LAQTHRDALTMSEDRPMLQFLLHTSFLSPLFILWLWTKPIARDFLHQPPFGETFSLLSDSA
FDSGRLWLLVVLCLLRLAVTRPHLQAYLCLAKARVEQLRREAGRIEAREIQQRVVRVYCYVT
VVSLQYLTPPLILTLNCTLLLKTLGGYSWGLGPAPLLSPDPSSASAAPIGSGEDEVQQTAARI
AGALGGLLTPFLRGVLAYLIWWTAACQLLASLFGLYFHQHLAGS

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FIGURE 145

CGTTNGCACGCGTCAATGGCGGTCTCGGAGTACAGCTGGTGGTGACCCCTGCTCACTGCCAC
CCTCATGCACAGGCTGGCGCCACACTGCTCCTTCGCGCGCTGGCTGCTCTGTAACGGCAGTT
TGTTCCGATACAAGCACCCGTNTTGAGGAGGAGCTCGGGCCCTGGCGGGGAAGCCGAGGCC
CAGAGGCAGGAAAGAGCGGTGGCCAATGGCCTTAGTGAGGAGAAGCCACTGTCTGTGCC
GAGATGCCCGTCCAGCTGGAGACCTGCCCCCTCACGACCGTGGATGCCCTGGCCTGCC
TTCTTCCTGGAGTACCAAGTGGTTGTGGACTTGCTGTACTCGGGCGCGTGTACCTCTT
CACAGAGGCCTACTACTACATGCTGGACCAGCCAAGGAGACTAACATTGCTGTGTTCTGGT
GCCTGCTCACAGTGACCTCTCCATCAAGATGTTCCCTGACAGTGACACGGCTGTACTCAGC
GCCGAGGAGGGGGGTGAGCGCTCTGCTGCCTCACCTTGCCCTTCCTGCTGCTGGC
CATGCTGGTGCAAGCG

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FIGURE 146

GGTCCTACATCCTCATCTGAGAATCAGAGAGCATAATCTTACGGGCCGTGATTTATTAACGTGGCCTTAAAGGAGC
AATCTGAAGGTCTCAGTCAAATTCTTGTATCTACTGATTGTGGGGCATGGCAAGGTTGCTTAAAGGAGC
TTGGCTGGTTGGCCCTTGTAGCTGACAGAAGGTGGCAGGGAGAATGCAGCACACTGCTCGGAGAATGAAGG
CGCTCTGTTGCTGGCTTGGCTCAGTCTGCTAACTACATTGACAATGTGGCAACCTGCACTTCTG
TATTGAGAACTCTGAAAGGTGCCTCCACTACGGCCTGACCAAAGATAGGAAGAGGGCGCTCACAAGATGGCTG
TCCAGACGGCTGTGCAGGCTCACAGCCACGGCTCCCTCCCCAGAGGTTCTGCAGCTGCCACCATCTCTTAA
TGACAGACGAGCCTGGCCTAGACAACCCCTGCTACGTGTCCTCGGCAGAGGACGGGAGCCAGCAATCAGCCCA
GTGGACTCTGGCCGGAGCAACCGAAGTGGCAGGGCCCTTGAGAGATCCACTATTAGAAGCAGATCATTAA
AAAAATAAATCAGACTTGTAGTCTCGAAGGACAAGAGCGGGAGTGCAGTTGCAACCATGCCGACCAGG
GCAGGGAAAATTCTGAAAACACCACTGCCCCCTGAAGTCTTCAAGGTTGATCCACCTGATTCCAGATGGTGA
ATTACCAAGCATCAAGATCAATCGAGTAGATCCCAGTGAAGGCCCTCTCTATTAGGCTGGAGGTAGCGAAC
CCCACGGTCCATATCATTATCAACACATTATCGTGATGGGTGATCGCCAGAGACGGCCGGCTACTGCCAG
GAGACATCATTCTAAAGGTCACGGGATGGACATCAGCAATGTCCTCACAACACTACGCTGTGCGTCTCTGCG
CAGCCCTGCCAGGTGCTGTGGCTGACTGTGATGCCAGAAGTCCCGCAGCAGGAAACATGGACAGGCC
GGATGCCCTACAGACCCCGAGATGACAGCTTCTGATGTGATCTCAACAAAAGTAGCCCCGAGGAGCAGCTTGGAA
TAAAACGGTGCAGGAGATGACCGTGTGTTAGCCATCAATGGACATGATCTCGATATGGCAGGCCAGAAAG
TGCGGCTCATCTGATTCAAGGCCAGTGAAGAGACGTGTTACCTCGTGTCCCGCCAGGTTCGGCAGGGAGCC
CTGACATCTTCAGGAAGCCGGCTGGAACAGCAATGGCAGCTGGTCCCAGGGCAGGGGAGAGGAGCAACACT
CCCAAGCCCCCTCCATCTACAATTACTGTATGAGAAGGTGTTAAATATCCAAAAGACCCGGTGAATCTCT
CGGCATGACCGTCGCAGGGGGAGCATACTACATAGAGAATGGGATTGCTATCTATGTCATCAGTGTGAGCCCG
GAGGAGTCATAAGCAGAGATGGAAGAATAAAACAGGTGACATTGGTGAATGTGGATGGGTGCAACTGACA
GAGGTGAGCCGGAGTGGAGGCAGTGGCATTATTGAAAAGAACATCATCTCGTGTACTCAAAGCTTGGAA
CAAAGAGTATGAGCCCCAGGAAGACTGCAGCAGCCAGCAGCCCTGGACTCCAACCACATGGCCCCACCA
GTGACTGGTCCCCATCTGGTCTGTTGGAATTACACCGGTCTGTATAACTGTAAAGATATTGTATA
CGAAGAAACACAGCTGGAGTCTGGCTCTGCAATTGAGGTTATGAAAGAATACAATGGAAACAAACCTT
TTTCATCAAATCCATTGTTGAAGGAACACCAGCATACAATGATGGAAGAATTAGATGTGGTGAATTCTCTG
CTGCAATGGTAGAAGTACATCAGGAATGATACATGCTGGCAAGACTGCTGAAAGAACTAAAGGAAGA
ATTACTCTAATATTGTTCTTGGCTGGCACTTTTATAGAATCAATGATGGGTCAAGAGGAAACAGAAAAAA
TCACAAATAGGCTAAGAAGTGAACACTATATTATCTGTCAGTTTATATTAAAGAAAGAATACATTGT
AAAAATGTCAGGAAAAGTATGATCATCTAAATGAAAGCCAGTTACACCTCAGAAAATATGATTCAAAAAA
AAACTACTAGTTTTTCTAGTGTGGAGGATTCTCATTACTCTACAACATTGTTATATTCTTCTATTCAAT
AAAAAGCCCTAAAACAACAAAATGATTGATTGATTTGATACCCCACTGAATTCAAGCTGATTTAAATTAA
GGTATATGCTGAAGTCTGCCAAGGGTACATTATGCCATTAACTTACAGCTAAATATTCTTAAATGCA
TTGCTGAGAACCGTGTGCTTCAACACAAGAATAATATTCTCAGAAGTTAA

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FIGURE 147

MKALLLLVLPWLSPANYIDNVGNLHFLYSELCKGASHYGLTKDRKRRSQDGCPDGASLTAT
APSPEVSAATISLMTDEPGLDNPAYVSSAEDGQPAISPVDGSRSNRTRARPFERSTIRSRS
FKKINRALSVLRRTKSGSAVANHADQGRENSENTTAPEVFPRLYHLIPDGEITSIKINRVDP
SESLSIRLVGGSETPLVHIIQHIYRDGVIARDGRLLPGDIILKVNMGMDISNVPHNYAVRLL
RQPCQVLWLTVMREQKFRSRNNQAPDAYRPRDDSFHVILNKSSPEEQLGIKLVRKVDEPGV
FIFNVLDGGVAYRHGQLEENDRVLAINGHDLRYGSPESAHLIQASERRVHLVVSQRQVQRS
PDIFQEAGWNSNGSWSPGPERSNTPKPLHPTITCHEVVNIQKDGPESLGMTVAGGASHRE
WDLPIYVISVEPGGVISRDGRIKTGDILLNVDGVELTEVRSEAVALLKRTSSSIVLKALEV
KEYEPQEDCSSPAALDSNHNMAPPSDWPSWVMWLELPRCLYNCKDIVLRRNTAGSLGFCIV
GGYEEYNGNKPFFIKSIVEGTPAYNDGRIRCGDILLAVNGRSTSGMIHACLRLLKELKGRI
TLTIVSWPGTFL

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FIGURE 148

CCAAAGTGATCATTGAAAAAGAGATATCCACATCTTCAAGCCATATAAAGGATAGAAGCT
GCACAGGGCAGCTTACTTACTCCAGCACCTCCTCTCCCAGGC~~AA~~**ATGG**TGCTGACCATCT
TTGGGATACAATCTCATGGATACGAGGTTTAACATCATCAGCCAAAGCAACAATGGTGGC
AATGTTCAGGAGACAGTGACAATTGATAATGAAAAAAATACGCCATCGTTAACATCCATGC
AGGATCATGCTCTTCTACCACAATTGGTACTATAAACATGGCTACATTGCATCCAGGGTGC
TCTCCCGAAGAGCCTGCTTATCCTGAAGATGGACCATCAGAACATCCCTCCTGAACAAT
CTCCAATGGTACATCTATGAGAACACAGGCTCTGGACAACATGTTCTCCAACAAATACACCTG
GGTCAAGTACAACCCTCTGGAGTCTCTGATCAAAGACGTGGATTGGTTCTGCTGGTCAC
CCATTGAGAAAATCTGCAAACATATCCCTTGTATAAGGGGAAGTGGTTGAAAACACACAT
AATGTCGGTGCTGGAGGCTGTGCAAAGGCTGGCTGGCATCTGGGAATTCAATCTG
TGCAGACATTCATGTT**AGG**ATGATTAGCCCTCTGTTATCTTCAAAGAAATACATCC
TTGGTTTACACTCAAAGTCAAATTAAATTCTTCCAATGCCCAACTAATTGAGATT
AGTCAGAAAATATAATGCTGTATTATA

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FIGURE 149

MKILVAFLVVLTIFGIQSHGYEVFNIISPSNNGGNQETVTIDNEKNTAIVNIHAGSCSSTT
IFDYKHGYIASRVLSSRACFILKMDHQNIPLNNLQWYIYEKQALDNMFSNKYTWVKYNPLE
SLIKDWDWFLLGSPIEKLCKHIPLYKGEVVENTHNVGAGGCAKAGLLGILGISICADIHV

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FIGURE 150

GGCACGAGCCAGGAACTAGGAGGTTCTCACTGCCCGAGCAGAGGCCCTACACCCACCGAGGC
ATGGGCTCCCTGGCTGTTCTGCTTGGCGTGCTGGCTGCCAGCAGCTCTCCAAGGCACG
GGAGGAAGAAATTACCCCTGTGGTCTCCATTGCCTACAAAGTCTGGAAGTTTCCCCAAAG
GCCGCTGGGTGCTCATAACCTGCTGTGCACCCCAGCCACCACCGCCCACACCTATTCCCTC
TGTGGAACCAAGAACATCAAGGTGGCAAGAAGGTGGTGAAGACCCACGAGCCGGCTCCTT
CAACCTAACGTCACACTCAAGTCCAGTCCAGACCTGCTCACCTACTTCTGCCGGGCGTCCT
CCACCTCAGGTGCCCATGTGGACAGTGCCAGGCTACAGATGCACTGGGAGCTGTGGTCCAAG
CCAGTGTCTGAGCTGCCGGCCAACTTCACTCTGCAGGACAGAGGGCAGGCCAGGGTCCAAG
GATGATCTGCCAGGCGTCTCGGGCAGCCCACCTATCACCAACAGCCTGATCGGGAAAGGATG
GGCAGGTCCACCTGCAGCAGAGACCATGCCACAGGCAGCCTGCCAACTTCTCCTCGCC
AGCCAGACATCGGACTGGTTCTGGTGCCAGGCTGCAAACAAACGCCAATGTCCAGCACAGCGC
CCTCACAGTGGTCCCCCAGGTGGTGACCAGAAGATGGAGGACTGGCAGGGTCCCTGGAGA
GCCCATCCTGCCCTGCCGCTCTACAGGAGCACCCGCCGTGAGTGAAGAGGAGTTGGG
GGGTTCAAGGATAGGAAATGGGAGGTCAAGGGACGCAAAGCAGCAGCCATG**TAG**ATGAACC
GTCCAGAGAGCCAAGCACGGCAGAGGACTGCAGGCCATCAGCGTGCAGTGGTGTATTTGGA
GTTCATGCAAAATGAGTGTGTTAGCTGCTTGGCACAAAAAAAAAAAAAA

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FIGURE 151

MGLPGLFCLAVLAASSFSKAREEEITPVVSIAYKVLEVFPKGRWVLITCCAPQPPPITYSL
CGTKNIKVAKKVVKTHEPASNVLNKSSPDLLTYFCRASSTSGAHVDSARLQMHWELWSK
PVSELRANFTLQDRGAGPRVEMICQASSGSPPITNSLIGKDGQVHLQQRPCHRQPANFSFLP
SQTSWDWFWCQAANNANVQHSALTVVPPGGDQKMEDWQGPLESPILALPLYRSTRRLSEEEFG
GFRIGNGEVRGRKAAAM

Signal Peptide:

amino acids 1-18

N-glycosylation Sites:

amino acids 86-89, 132-135, 181-184

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FIGURE 152

GGTCCTTAATGGCAGCAGCCGCCGCTACCAAGATCCTTCTGTGCCTCCCGCTTCTGCTCCTG
CTGTCCGGCTGGTCCCAGGGCTGGCGAGCCGACCCCTCACTCTCTTGCTATGACATCACCCTG
CATCCCTAAGTTCAAGACCTGGACCACGGTGGTGTGCGGTTCAAGGCCAGGTGGATGAAAAGA
CTTTTCTTCACTATGACTGTGGCAACAAGACAGTCACACCTGTCAGTCCCCTGGGAAGAAA
CTAAATGTCACAACGGCCTGGAAAGCAGACAGAACCCAGTACTGAGAGAGGGTGGTGGACATACT
TACAGAGCAACTGCGTGACATTCACTGGAGAATTACACACCCAAGGAACCCCTCACCTGC
AGGCAAGGATGTCTTGTGAGCAGAAAGCTGAAGGACACAGCAGTGGATCTGGCAGTTCACT
TTCGATGGGCAGATCTCCTCCTTCACTCAGAGAAGAGAATGTGGACAACGGTTCATCC
TGGAGCCAGAAAGATGAAAGAAAAGTGGGAGAATGACAAGGTGTGGCCATGTCCTCCATT
ACTTCTCAATGGGAGACTGTATAGGATGGCTTGAGGACTTCTTGATGGCATGGACAGCACC
CTGGAGCCAAGTGCAGGAGCACCACCTGCCATGTCCTCAGGCACAACCCAACTCAGGGCCAC
AGCCACCACCCCTCATCCTTGCTGCCTCCTCATCATCCTCCCTGCTTCATCCTCCCTGGCA
TCTGAGGAGAGTCCTTAGAGTGACAGGTTAAAGCTGATACAAAAGGCTCTGTGAGCACG
GTCTTGATCAAACCTGCCCTTCTGTCTGGCCAGCTGCCACGACCTACGGTGTATGTCCAGT
GGCCTCCAGCAGATCATGATGACATCATGGACCCAAAGCTCATTCACTGCCTTGATTCCCT
TTGCCAACAAATTACCAAGCAGTTACCTAACATATTATGCAATTTCCTTGTGCTTAC
TGATGGAATTCCCTGCACTTAAAGTTCTGGCTGACTAAACAAGATATATCATTTCCTTCTTCC
TCTTTTGTGAAATCAAGTACTTCTTGATGATGATCTCTTCTTGCAAATGATATT
GTCAGTAAATAATCACGTTAGACTTCAGACCTCTGGGATTCTTCCGTGCTGAAAGAG
AATTTTAAATTATTAATAAGAAAAAATTATATTAAATGATTGTTCTTGTAGAATTTAT
TGTCTGACTGATATTAAATAAGAGTTCTATTCCCCAAAAAAAAAAAAAA

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FIGURE 153

MAAAAATKILLCLPLLLLGSWSRAGRAPHSLCYDITVIPKFRPGPRWCAYQQVDEKTFHYD
DCGNKTVTPVSPLGKKLNVTAWKAQNPNLREVVVDILTEQLRDIQLENYTPKEPLTLQAR
MSCEQKAEGHSSGSWQFSFDGQIFLLFDSEKRMWTTVHPGARKMKEKWENDKVVAMSFHYS
MGDCIGWLEDFLMGMDSTLEPSAGAPLAMSSGTTQLRATATTLILCCLIIILPCFILPGI

Important features:**Signal peptide:**

amino acids 1-25

Transmembrane domain:

amino acids 224-246

N-glycosylation site.

amino acids 68-72, 82-86

N-myristoylation site.

amino acids 200-206, 210-216

Amidation site.

amino acids 77-81

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FIGURE 154

GGGAAAGCCATTCGAAAACCATCTATACAAACTATATATTTCAATTCTGCTGCTAGCTG
CCTTGGGCCTCACAAATTCATTCTGTTCTGACTTCAGTTATATACCGTGAATGGAG
TTGATCCCAACCATAACATCGTGGAGGGTTTAATTTGGTAGCCCTCACCCAAATTCTG
GTGTGGCTTCTTGAGAGGATTCCACCTCAAAATCATGAACCTGGCTGTTGATCAAAA
GAGAATTGGATTCTACTCTAAAAGTCATATAGGACTTGGCAAAAGAAGCTAGCAGAAGAC
TCAACCTGGCCTCCCATAACAGGACAGATTTCAGGTGATGGCAAAATGGATTCTACAT
CAACGGAGGCTATGAAAGCCATGAACAGATTCCAAAAAGAAAACCAAATTGGGAGGCCAAC
CCACAGAACAGCATTCTGGGCCAGGCTGTAATCAGAATTGTCGTCGTACATGCTAACAGC
ATTGCTTTTCCCCAAAATTAAACACATTGTGGAGAAGTGATGATACTCTCCCCTTACCTT
CCTCTCTCCATTCAAGCATTCAAAGTATATTTCAATGAATTAAACCTTGCAGCAAGGGACC
TTAGATAGGCTTATTCTGACTGTATGCTTACCAATGAGAGAAAAAAATGCATTCTGTAT
CATCCTTTCAATAAACTGTATTCAATTGGAAAAAAAAAAAAAA

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FIGURE 155

MELIPTITSWRVLILVVALTQFWCGFLCRGFHLQNHELWLLIKREFGFYSKSQYRTWQKKLA
EDSTWPPINRTDYSGDGKNGFYINGGYESHEQIPKRKLKLGGQPTEQHFWARL

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FIGURE 156

GTTCTCCTTCCGAGCCAAATCCCAGGCGATGGTGAATTATGAACGTGCCACACC**ATGAAG**
CTCTTGTGGCAGGTAACTGTGACCCACACCTGGAATGCCATCCTGCTCCCCTCGTCTA
CCTCACGGCGCAAGTGTGGATTCTGTGTCAGCCATCGCTGCTGCCGCTCAGCCGGGCCCC
AGAACTGCCCTCCGTTGCTCGTGCAGTAACCAGTTCAAGCAAGGTGGTGTGCACGCGCCGG
GGCCTCTCCGAGGTCCCGCAGGGTATTCCCTGAACACCCGGTACCTCAACCTCATGGAGAA
CAACATCCAGATGATCCAGGCCGACACCTCCGCCACCTCCACCTGGAGGTCTGCAGT
TGGGCAGGAACTCCATCCGGCAGATTGAGGTGGGGCCTCAACGGCTGCCAGCCTCAAC
ACCCCTGGAGCTGTTGACAACTGGCTGACAGTCATCCCTAGGGGGCCTTGAATACCTGTC
CAAGCTGCCGGAGCTCTGGCTCGAACAAACCCATCGAAAGCATCCCTCTACGCCCTCA
ACCGGGTGCCCTCCCTCATGCCCTGGACTGGGGAGCTCAAGAAGCTGGAGTATATCTCT
GAGGGAGCTTTGAGGGGCTGTTCAACCTCAAGTATCTGAACCTGGGATGTGCAACATTAA
AGACATGCCAATCTACCCCCCTGGTGGGCTGGAGGAGCTGGAGATGTCAAGGAACCACT
TCCCTGAGATCAGGCCCTGGCTCCTCATGGCCTGAGCTCCCTCAAGAAGCTGGGTCTG
AACTCACAGGTCAAGCTGATTGAGCGGAATGCTTGAACGGGCTGGCTCATTGTGGAAC
CAACTGGCCCACAATAACCTCTTCTTGCCTCATGACCTCTTACCCGCTGAGGTACC
TGGTGGAGTGCATCTACACCACAACCCCTGGAACGTGTGATTGTGACATTCTGTGGCTAGCC
TGGTGGCTCGAGAGTATATACCCACCAATTCCACCTGCTGTGGCGCTGTATGCTCCCAT
GCACATGCGAGGCCGCTACCTCGTGGAGGTGGACCAGGCCTCTCCAGTGCTCTGCCCCCT
TCATCATGGACGCACCTCGAGACCTCAACATTCTGAGGGTCGGATGGCAGAACATTAGTGT
CGGACTCCCCCTATGCTCTCCGTGAAGTGGTGCTGCCAATGGGACAGTGCTCAGGCCACGC
CTCCCGCCACCCAAGGATCTCTGCTCAACGACGGCACCTGAACTTTCCCACGTGCTGC
TTTCAGACACTGGGGTGTACACATGCATGGTGACCAATGTTGCAAGGCAACTCCAACGCC
GCCTACCTCAATGTGAGCACGGCTGAGCTAACACCTCAACTACAGCTCTTACCAACAG
AACAGTGGAGGACACGGAGATCTCGCCTGAGGACACAACGCGAAAGTACAAGCCTGTTCTA
CCACGTCACACTGGTTACAGCCGGCATATACCACCTCTACCACGGTGCTCATTGACTACC
CGTGTGCCAAGCAGGTGGCAGTACCCGGACAGACACCACTGACAAGATGCAGACCAGCCT
GGATGAAGTCATGAAGGACCAAGATCATCATTGGCTGCTTGTGGCAGTGACTCTGCTAG
CTGCCGCATGTTATTGTCTTCTATAAAACTTCGTAAGCGGACCGAGCAGGGAGTACAGTC
ACAGCCGCCGGACTGTTGAGATAATCCAGGTGGACGAAGACATCCAGCAGCACATCCGC
AGCAGCAACAGCAGCTCCGTCCGGTGTATCAGGTGAGGGGGCAGTAGTGCTGCCACAATT
ATGACCATATTAACTACAACACTACAAACCAGCACATGGGCCACTGGACAGAAAACAGC
CTGGGGAACTCTCTGCACCCACAGTCACCACTATCTGAAACCTTATATAATTGACACCA
TACCAAGGACAAGGTACAGGAAACTCAAAT**TGA**CTCCCTCCCCAAAAAAACTATAAAAT
GCAATAGAATGCACACAAAGACAGCAACTTTGTACAGAGTGGGGAGAGACTTTTCTGTA
TATGCTTATATATTAAGTCTATGGCTGGTAAAAAAACAGATTATATTAAAATTAAAGA
CAAAAGTCAAAACA

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FIGURE 157

MKLLWQVTVHHHTWNAILPFVYLTAQWILCAAIAAAASAGPQNCPSVCSCSNQFSKVVC
RRGLSEVPQGIPSNTTRYLNLMENNIQMIQADTFRHLHLEVLQLGRNSIRQIEVGAFNGLAS
LNTLELFDNWLTVIPSGAFEYLSKLRELWLRNNPIESIPSYAFNRVPSLMRLDLGELKKLEY
ISEGAFEGFLNLKYLNLCMCNIKDMNPNTPLVGLEELEMMSGNHFPEIRPGSFHGLSSLKKLW
VMNSQVSLIERNAFDGLASLVELNLAHNNLSSLPHDLFTPLRYLVELHLHHNPWNCDCDILW
LAWWLREYIPTNSTCCGRCHAPMHMRGRYLVEVDQASFQCSAPFIMDAPRDLNISEGRMAEL
KCRTPPMSSVKWLLPNGTVLSHASRHPRI SVLNDGTLNFHVLLSDTGVYTCMVTVAGNSN
ASAYLNVSTAELNTSNYSFFT TVT VETTEISPEDTTRKYKPVPTTSTGYQPAYTTSTVLIQ
TTRVPKQVAVPATDTDKMQTSLDEVMKTTKIIIGCFVAVTLLAAAMLIVFYKLRKRHQQRS
TVTAARTVEIIQVDEDIPAATSAATAAPSGVSGE GAVVLPTIHDHINYNTYKPAHGAHWE
NSLGNSLHPTVTTISEPYIIQTHTKDKVQETQI

FIGURE 158

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FIGURE 159

MELGCWTQLGLTFLQLLLISSLPREYTVINEACPGAEWNIMCRECCCEYDQIECVCPGKREVV
GYTIPCCRNEENECDSCLIHPGCTIFENCKSCRNGSWGGTLDDFYVKGFYCAECRAGWYGGD
CMRCGQVLRAPKGQILLESYPLNAHCEWTIHAKPGFVIQLRFVMLSLEFDYMCQYDYVEVRD
GDNRDGQIIKRVCGNERPAPIQSIGSSLHVLFHSDGSKNFDGFHAIYEEITACSSSPCFHDG
TCVLDKAGSYKCACLAGYTGQRCENLLEERNCSDPGGPVNGYQKITGGPGLINGRHAKIGTV
VSFFCNNSYVLSGNEKRTCQQNGEWSGKQPICIKACREPKİSDLVRRRVLPMQQSRETPLH
QLYSAAFSKQKLQSAPTKKPALPFGDLPMGYQHLHTQLQYECISPFYRRLGSSRTCLRTGK
WSGRAPSCIPICGKIENITAPKTQGLRWPWQAAIYRRRTSGVHD GSLHKGAWFLVCSGALVNE
RTVVVAAHCVTDLGKVTMIKTADLKVLGKFYRDDRDEKTIQSLQISAIILHPNYDPILLD
ADIAILKLLDKARISTRVQPICLAASRDLSTS FQESHITVAGWNVLADVRSPGFKNDSLRSG
VVSVVDSLLCEEQHEDHGI PVSVDNMFCASWEPTAPS DICTAETGGIAAVSFPGGRASPEPR
WHLMGLVWSWSYDKTCSHRLSTAFTKVLFKDWIERNMK

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FIGURE 160

ACCAGGCATTGTATCTCAGTTGTCATCAAGTCGCAATCAGATTGGAAAAGCTCAACTTGA
AGCTTTCTTGCCTGCAGTGAAGCAGAGAGATAGATATTATTACGTAATAAAAACATGGGC
TTCAACCTGACTTCCACCTTCTACAAATTCCGATTACTGTTGCTGTTGACTTGTGCCT
GACAGTGGTTGGGTGGGCCACCAGTAACACTACTTCGTGGTGCCATTCAAGAGATTCCTAAAG
CAAAGGAGTCATGGCTAATTCCATAAGACCCCTATTTGGGAAAGGGAAAAACTCTGACT
AATGAAGCATCCACGAAGAAGGTAGAACACTGACAACACTGTCCTCTGTGTCCTACCTCAG
AGGCCAGAGCAAGCTCATTCAAACCAAGATCTCACTTGAAGAGGTACAGGCAGAAAATC
CCAAAGTGTCCAGAGGCCGGTATGCCCTCAGGAATGTAAGCTTACAGAGGGTCGCCATC
CTCGTCCCCACCGAACAGAGAGAAACACCTGATGTACCTGCTGGAACATCTGCATCCCT
CCTGCAGAGGCAGCAGCTGGATTATGGCATCTACGTATCCACCAGGCTGAAGGTAAAAAGT
TTAATCGAGCCAAACTCTTGAATGTGGCTATCTAGAACGCTCAAGGAAGAAAATTGGGAC
TGCTTATATTCCACGATGTGGACCTGGTACCCGAGAACATGACTTTAACCTTACAAGTGTGA
GGAGCATCCCAAGCATTGGTGGTGGCAGGAACAGCACTGGTACAGGTTACGTTACAGTG
GATATTGGGGTGTACTGCCCTAACGAGAGCAGTTCAAGGTGAATGGATTCT
AACAACTACTGGGATGGGGAGGCAGAGACGATGACCTCAGACTCAGGGTTGAGCTCCAAAG
AATGAAAATTCCCGCCCTGCCCTGAAGTGGTAAATATAACATGGTCTTACACTAGAG
ACAAAGGCAATGAGGTGAACGCAGAACGGATGAAGCTCTAACCAAGTGTACAGGACTGG
AGAACAGATGGGTTGAGTAGTTGTTCTATAAATTAGTATCTGTGGAACACAATCCTTATA
TATCAACATCACAGTGGATTCTGGTTGGCATGACCCCTGGATCTTGGTATGTTGG
AAGAACTGATTCTTGTGCAATAATTGGCCTAGAGACTTCAAATAGTAGCACACATTA
AGAACCTGTTACAGCTCATTGTTGAGCTGAATTTCCTTTGTATTCTTAGCAGAGCT
CCTGGTGTAGAGTATAAACAGTTGTAACAAGACAGCTTCTTAGTCATTGATCATG
AGGGTTAAATATTGTAATATGGACTTGAAGGACTTATATAAAAGGATGACTCAAAGGAT
AAAATGAACGCTATTGAGGACTCTGGTTGAAGGAGATTATTAAATTGAAAGTAATATAT
TATGGATAAAAGGCCACAGGAAATAAGACTGCTGAATGTCAGAGAACAGAGTTGTTCT
CGTCCAAGGTAGAAAGGTACGAAGATAACAATACTGTTATTCAATTATCCTGTACAATCATCT
GTGAAGTGGTGGTGTCAAGGTGAGAAGGCCACAAAAGAGGGAGAAAAGGCGACGAATCA
GGACACAGTGAACCTGGGAATGAAGAGGTAGCAGGAGGGTGGAGTGTGCGCTGCAAAGGCAG
CAGTAGCTGAGCTGGTTGCAGGTGCTGATAGCCTTCAGGGGAGGACCTGCCAGGTATGCCT
TCCAGTGTGATGCCACCAGAGAATACATTCTATTAGTTAAAGAGTTTGAAATGA
TTTGTCAGTACAAGTAGGATATGAATTAGCAGTTACAAGTTACATATTAACATAATAAAATA
TGTCTATCAAATACCTCTGTAGTAAAATGTAAAAAGCAAAA

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FIGURE 161

MGFNLTFHLSYKFRLLLLLTLCLTVVGWATSNYFVGAIQEIPKAKEFMANFHKTLLGKGKT
LTNEASTKKVELDNCPSVSPYLRGQSKLIFKPDLTLEEVQAENPKVSRGRYRPQECKALQRV
AILVPHRNREKHLMYLLEHLHPFLQRQQLDYGIYVIHQAEGKKFNRAKLLNVGYLEALKEEN
WDCFIFHDVDLVPENDFNLYKCEEHPKHLVVGRNSTGYRLRYSGYFGGVTA
LSREQFFKVNG
FSNNYWGWGGEDEDDLRLRVELQRMKISRPLPEVGKYTMVFHTRDKGNEVNAERMKLLHQVSR
VWRTDGLSSCSYKLVSVEHNPLYINITVDFWFGA

Important features:

Signal peptide:

amino acids 1-27

N-glycosylation sites:

amino acids 4-7, 220-223 and 335-338

Xylose isomerase proteins:

amino acids 191-201

FIGURE 162

CGTGGGCCGGGGTCGCGCAGCGGGCTGTGGGCGGCCGGAGGAGCGACCGCCGCAGTTCTC
GAGCTCCAGCTGCATTCCCTCCGCGTCCGCCACGCTTCTCCGCTCCGGCCCCGCA**ATG**
GCCCAGGCAGTGTGGTCGCGCCTCGGCCGATCCTCTGGCTTGCTGCCTCTGCCCTGGG
CCCGGCAGGGTGGCCGAGGCCTGTATGAACCTAACATCTACCAACCGATA
CGGGAGCGGTGGTGGACCATCTCGCCAGCCTGGCAAGGACAACGGCAGCCTGCCCTG
CCCGCTGACGCCACCTTACCGCTTCACTGGATCCACACCCCCGCTGGTGCCTACTGGAA
GATGGAGAAGGGTCTCAGCTCACCATCCGTGTGGTCGGCACGTGCCGGGAATTCCCG
TCTCTGTCTGGGTCACTGCCGCTGACTGCTGGATGTGCCAGCCTGTGGCAAGGGCTTGTG
GTCCTCCCCATCACAGAGTTCTCGTGGGGACCTTGTGTCACCCAGAACACTTCCCTACC
CTGGCCCAGCTCTATCTACTAACAGACCGTCTGAAAGTCTCCTCCACGACCCGA
GCAACTCCTCAAGACCCCTTGTTCCTACAGCTGGACTTCGGGACCTTACCGTGAAGCT
GTGACTGAAGACTCCGTGGTCTATTATAACTATTCCATCATCGGACCTTACCGTGAAGCT
CAAAGTGGTGGCGGAGTGGGAAGAGGGTGGAGGCCGATGCCACGAGGGCTGTGAAGCAGAAGA
CCGGGACTTCTCCGCCTCGCTGAAGCTGCAGGAACCTTCGAGGCATCCAAGTGTGGGG
CCCACCTAATTAGACCTCCAAAAGATGACCGTGACCTTGAACTTCTGGGAGCCCTCC
TCTGACTGTGTGCTGGCTCAAGCCTGAGTGCTCCGCTGGAGGAAGGGAGTGCCACC
CTGTGTCGCGTGGCCAGCACAGTACAACCTGACCCACACCTTCAGGGACCTGGGACTAC
TGCTTCAGCATCAGGGCGAGAATATCATCAGCAAGACACATCAGTACCAACAAGATCCAGGT
GTGGCCCTCCAGAATCCAGCGGCTGTCTTGCTTCCATGTCTACACTTACACTGTGA
TGTTGGCCTTCATCATGTACATGACCCCTGCGGAATGCCACTCAGCAAAGGACATGGTGGAG
AACCCGGAGCCACCCCTGGGTCAAGGTGCTGCTGCCAGATGTGCTGTGGCCTTCTGCT
GGAGACTCCATCTGAGTACCTGGAAATTGTTCTGTGAGAACACACGGGCTGCTCCGCCCTCT
ATAAGTCTGCAAAACTACACCGTGT**G**ACTCCCTCCACCCATCTCAGTGTAA
CTGACTGCTGACTTGGAGTTCCAGCAGGGTGGTGTGACCACTGACCAGGAGGGTTCAATT
TGCCTGGGCTGTTGGCCTGGATCATCCATCCATCTGTACAGTTCAGCCACTGCCACAAGCC
CCTCCCTCTGTCAACCCCTGACCCAGCCATTCAACCATCTGTACAGTCCAGCCACTGACA
TAAGCCCCACTCGGTTACCAACCCCTGACCCCTACCTTGAAAGAGGCTCGTGCAGGACT
TTGATGCTTGGGTGTTCCGTGTTGACTCTAGGTGGCCTGGCTGCCACTGCCATTCT
CTCATATTGGCACATCTGCTGTCATTGGGGTTCTCAGTTCTCCCTCCACAGACGCCCTAC
CTGTGCCAGAGAGCTAGAAAGAAGGTCAAAAGGGTTAAAATCCATAACTAAAGGGTGTAC
ACATAGATGGGCACACTCACAGAGAGAAGTGTGCATGTACACACACCACACACACACA
CACACACACAGAAATATAACACATGCGTCACATGGCATTTCAGATGATCAGCTGT
TCTGGTTAAGTGGTGTGGATGCACCCCTGCACTAGAGCTGAAAGGAAATTGACCTCCA
AGCAGCCCTGACAGGTTCTGGGCCGGGCCCTCCATTGTGCTTGTCTGCAGTCTTGC
GCCCTTATAAGGCCATCCTAGTCCCTGCTGGCTGGCAGGGGCCGGATGGGGGGCAGGACT
AAATACTGAGTATTGCAAGAGTGTCTTATAAAATACACCTTATTTATC
GAAACCCATCTGTGAAACTTCACTGAGGAAAGGCCTTGCAAGCGTAGAAGAGGTTGAGTCAAGGCCGGCG
TGGCTACGCCCTGTAATCCAGCATTGGGAGGCCAGGCGGGTGGATCACGAGATCAGGA
GATCGAGACCACCCCTGGCTAACACCGTGAAACCCCGTCTACTAAAAAAATACAAAAAGTT
AGCCGGCGTGGTGGTGGCTGTAGTCCAGCTACTCGGGAGGCTGAGGCAGGAGAATG
GTGCGAACCCGGAGGCAGCTTGCAGTGAGGCCAGATGGCGCCACTGCACCTCAGCCTGA
GTGACAGAGCGAGACTCTGTCTCCA

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FIGURE 163

MAQAVWSRLGRILWLACLLPWAPAGVAAGLYELNLTTDSPATTGAVVTISASLVAKDNGSLA
LPADAHLYRFHWIHTPLVLTGKMEKGLSSTIRVVGHPGEFPVSVWVTAADCWMCQPVARGF
VVLPITEFLVGLVVTQNTSLPWPSYYLTKTVLKVSFLLHDPSNFLKTALFLYSWDFGDGTQ
MVTEDSVVYYNYSIIGTFTVKLVVAEWEVEPDATRAVKQKTGDFSASLKLQETLRGIQVL
GPTLIQTFQKMTVTLNFLGSPPLTVCWRLKPECLPLEEGECHPVSVASTAYNLHTFRDPGD
YCFSIRAENIISKTHQYHKIQVWPSRIQPAVFAPCATLITVMLAFIMYMTLRNATQQKDMV
ENPEPPSGVRCQCQMCQCGPFLLETPSEYLEIVRENHGLLPPLYKSVKTYTV

Important features of the protein:

Signal peptide:

amino acids 1-24

Transmembrane domain:

amino acids 339-362

N-glycosylation sites.

amino acids 34-37, 58-61, 142-145, 197-200, 300-303 and 364-367

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FIGURE 164

GCTCAAGACCCAGCAGTGGGACAGCCAGACAGACGGCACGTGGACTGAGCTCCAGATCT
GGGCCGCTTGCCTCCTGCTCCTCCTCCTGCCAGCCTGACCAGTGGCTCTGTTTCCA
CAACAGACGGGACAACCTGCAGAGCTGCAACCCCAGGACAGAGCTGGAGCCAGGGCCAGCTG
GATGCCCATGTTCCAGAGGCGAAGGAGGCAGACACCCACTCCCCATCTGCATTTCTGCT
GCGGCTGCTGTCATCGATCAAAGTGTGGATGTGCTGCAAGACGTAGAACCTACCTGCCCTG
CCCCCGTCCCTCCCTCCTTATTATTCTGCTGCCAGAACATAGGTCTTCCAATAAAA
TGGCTGGTTCTTTGTTTCCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 165

MALSSQIWAACLLLLLLASLTSGSVFPQQTGQLAELQPQDRAGARASWMPMFQRRRRDTH
FPICIFCCGCCCHRSKCGMCCKT

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FIGURE 166

CTGTCAGGAAGGACCATCTGAAGGCTGCAATTGTTCTAGGGAGGCAGGTGCTGGCCTGGC
CTGGATCTTCCACCATGTTCTGTTGCTGCCTTTGATAGCCTGATTGTCAACCTCTGGC
ATCTCCCTGACTGTCCTCTCACCCCTCTCGTTTACATCATAGTGCAGCCATTGG
AGTCTCCTTGGTATCCGCAAACCTACATGAAAAGTCTGTAAAAATCTTGCCTGGGCTA
CCTTGAGAATGGAGCGAGGAGCCAAGGAGAAGAACCAACAGCTTACAAGCCCTACACCAAC
GGAATCATTGCAAAGGATCCCACACTAGAAGAAGAGATCAAAGAGATTGCGAAGTGG
TAGTAGTAAGGCTCTGGACAACACTCCAGAGTTCGAGCTCTGACATTCTACTTTGCC
GGAAAGGAATGGAGACCATTATGGATGATGAGGTGACAAAGAGATTCTCAGCAGAAGAACTG
GAGTCCTGGAACCTGCTGAGCAGAACCAATTATAACTCCAGTACATCAGCCTCGGCTCAC
GGTCCTGTGGGGTTAGGAGTGCCTGATTCCAGTCTGCTGGTGGCACAACGTGTTGGGAACTTGCC
TGGCTTCACAGGGATTAGCCTCTGGTGGTGGGACAACGTGTTGGGAACTTGCCAAAT
GGGAGGTTAAGGAATTGAGTAAACATGTTCACTTAATGTGTTACCGGATCTGCGTGC
AGCGCTGACAGCCATCATCACCTACCATGACAGGGAAAACAGACCAAGAAATGGGCACT
GTGTGGCCAATCATACTCACCGATCGATGTGATCATCTTGGCCAGCGATGGCTATTATGCC
ATGGTGGGTCAAGTGCACGGGGACTCATGGGTGTGATTCAAGAGAGCCATGGTGAAGGCCTG
CCCACACGCTGGTTGAGCGCTCGGAAGTGAAGGATGCCACCTGGTGGCTAACAGAGACTGA
CTGAACATGTGCAAGATAAAAGCAAGCTGCCTATCCTCATCTTCCCAGAACGGAACTGCATC
AATAATACATCGGTGATGATGTCAAAAGGGAAAGTTGAAATTGGAGCCACAGTTACCC
TGGTGCATCAAGTATGACCCCTCAATTGGCGATGCCTCTGGAACAGCAGCAAATACGGGA
TGGTGACGTACCTGCTGCGAATGATGACCAAGCTGGCCATTGTCTGCAGCGTGTGGTACCTG
CCTCCCATGACTAGAGAGGCAGATGAAGATGCTGTCAGTTGCGAATAGGGTGAAATCTGC
CATTGCCAGGCAGGGAGGACTTGTGGACCTGCTGTGGATGGGGCCTGAAGAGGGAGAAGG
TGAAGGACACGTTCAAGGAGGAGCAGCAGAACAGCTGTACAGCAAGATGATGTCGGGAACCAC
AAGGACAGGAGCCGCTCTTGAGCTGCCCTCAGCTGGCTGGGCCACCGTGCAGGGTGC
CGGGCTCAGAGCTGGAGTTGCCGCCGCCACTGCTGTGCTTCCAGACTCCAGGG
CTCCCCGGGCTGCTGGATCCAGGACTCCGGCTTCGCCAGCGCAGCGGGATCCCTGT
GCACCCGGCGCAGCCTACCCCTGGTGTCTAAACGGATGCTGCTGGTGTGCAACCCAGGA
CGAGATGCCTTGTCTTACAATAAGTCGTTGGAGGAATGCCATTAAAGTGAACCTCCA
CCTTGACCGCTGTGCGGGCTGAGTGGTTGGGAGATGTGCCATGGTCTTGTGCTAGAGAT
GGCGGTACAAGAGTCTGTTATGCAAGCCGTGTGCCAGGGATGTGCTGGGGCGGCCACCCG
CTCTCCAGGAAAGGCACAGCTGAGGCAGTGGCTGGCTGGCTCCAGCTAACATGCC
CTTGGAGCTGCAAGACATGATAGGAAGGAAACTGTCATCTGCAGGGGCTTCAGCAAATG
AAGGGTTAGATTTTATGCTGCTGATGGGGTTACTAAAGGGAGGGAAAGAGGCCAGGTG
GGCCGCTGACTGGGCATGGGAGAACGTGTGTTGCTACTCCAGGCTAACCTGAACCT
ATGTGATGCCGCTTGTGAATGTGTCGTTCCCCATCTGTAATATGAGTCGGGG
GAATGGTGGTGATTCTACCTCACAGGGCTGTTGGGGATTAAGTGCTGCGGGTGAGTGA
AGGACACATCACGTTCAAGTACAGGCCACAAACGGGGCACGGCAGGCCTGAG
CTCAGAGCTGCTGCACTGGCTTGGATTGTTGTGAGTAAATAACTGGCTGGTGAA
TGA

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FIGURE 167

MFLLLPFDSLIVNLLGISLTVLFTLLLVIIVPAIFGVSGIRKLYMKSLKIFAWATLRME
RGAKEKNHQLYKPYTNGIIAKDPTSLEEEIKEIRRGSSKALDNTPEFELSDIFYFCRGME
TIMDDEVTKRFSAAELESWNLLSRTNMFQYISLRLTVLWGLGVLIRYCFLLPLRIALAFTG
ISLLVVGTTVVGYLPNGRFKEFMSKHVHLMCYRICVRALTAITYHDRENPRNGGICVANH
TSPIDVIILASDGYYAMVGQVHGLMGVIQRAMVKACPHWFERSEVKDRHLVAKRLTEHVQ
DKSKLPILIFPEGTCINNTSVMFKKGSFEIGATVYPVAIKYDPQFGDAFWNSSKYGMVTL
LRMMTSWAIVCSVWYLPPMTREADEDAVQFANRVKSAIARQGLVDLLWDGGLKREKVKDTF
KEEQQKLYSKMIVGNHKDRSRS

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FIGURE 168

GCCCCTCGAAACCAGGACTCCAGCACCTCTGGTCCC GCCCTCACCCGGACCCCTGGCCCTCA
CGTCTCCTCCAGGG**ATGG**CGCTGGCGGCTTGTGATGATGCCCTCGGCAGCCTCGGCCTCCAC
ACCTGGCAGGCCAGGCTGTTCCCACCATCCTGCCCTGGGCTGGCTCCAGACACCTTGAG
CGATAACCTATGTGGGTTGTGCAGAGGAGATGGAGGAGAAGGCAGCCCCCTGCTAAAGGAGG
AAATGGCCCACCATGCCCTGCTCGGGAATCCTGGGAGGCAGCCCAGGAGACCTGGGAGGAC
AAGCGTCGAGGGCTTACCTGCCCTGGCTCAAAGCCCAGAATGGAATAGCCATTATGGT
CTACACCAACTCATCGAACACCTGTACTGGGAGTTGAATCAGGCCGTGCGGACGGCGGAG
GCTCCCGGGAGCTCTACATGAGGCACCTCCCTCAAGGCCCTGCATTCTACCTGATCCGG
GCCCTGCAGCTGCTCGAGGCAGTGGGGCTGCAGCAGGGACCTGGGAGGTGGTGGTCCG
AGGTGTGGCAGCCTCGCTTGAAACCCAAAGAGGCTGGGGACTCTGTCCGCTGGGCCAGT
TTGCCTCCAGCTCCCTGGATAAGGCAGTGGCCCACAGATTGGGAGAAGAGGGGGCTGT
GTGTCTGCCAGGGGTGCAGCTAGGTACAATCTGAGGGGCCTCCTCTGCCCTTG
GAAGACTCTGCTTGGCCCTGGAGAGTTCCAGCTCTCAGGGGTTGGGCC**TGA**AAGTCCA
ACATCTGCCACTTAGGAGCCCTGGAACGGGTGACCTCATATGACGAAGAGGCACCTCCAG
CAGCCTTGAGAAGCAAGAACATGGTCCGGACCCAGCCCTAGCAGCCTCTCCCCAACCAGG
ATGTTGGCCTGGGAGGCCACAGCAGGGCTGAGGGAACTCTGCTATGTGATGGGACTTCCT
GGGACAAGCAAGGAAAGTACTGAGGCAGCCACTTGATTGAACGGTGGTCAATGTGGAGACA
TGGAGTTTATTGAGGTAGCTACGTGATTAATGGTATTGCAGTGTGGA

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FIGURE 169

MALAALMIALGSLGLHTWQAQAVPTILPLGLAPDTFDDTYVGCAEEMEEKAAPLLKEEMAH
ALLRESWEAAQETWEDKRRGLTLPPGFKAQNGIAIMVYTNSNTLYWELNQAVRTGGGSREL
YMRHFPPFKALHFYLIRALQLLRGSGGCSRGPGEVVFRGVGSLRFEPKRLGDSVRLGQFASSS
LDKAVAHRFGEKRRGCVSAPGVQLGSQSEGASSLPPWKTLLAPGEFQLSGVGP

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FIGURE 170

GTGGCTTCATTCAGTGGCTGACTTCCAGAGAGCAATATGGCTGGTCCCCAACATGCCTCA
CCCTCATCTATATCCTTGGCAGCTCACAGGGTCAGCAGCCTCTGGACCCGTGAAAGAGCTG
GTCGGTTCCGTTGGTGGGGCCGTGACTTCCCCCTGAAGTCAAAGTAAAGCAAGTTGACTC
TATTGTCTGGACCTTCAACACAACCCCTTGTCAACCACAGCCAGAAGGGGGCACTATCA
TAGTGACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCCAGATGGAGGCTACTCCCTGAAG
CTCAGCAAACGTGAAGAAGAATGACTCAGGGATCTACTATGTGGGGATATAACAGCTCATCACT
CCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACGAGCACCTGTCAAAGCCTAAAG
TCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTGACCAATCTGACATGCTGCATG
GAACATGGGAAGAGGATGTGATTTACCTGGAAGGCCCTGGGCAAGCAGCCAATGAGTC
CCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGAGAAAGTGTATGACCTTCATCT
GCGTTGCCAGGAACCTGTCAGCAGAAACTCTCAAGCCCCATCCTGCCAGGAAGCTCTGT
GAAGGTGCTGCTGATGACCCAGATTCCCTCATGGTCCTCTGTGTCTCCTGTTGGTGCCT
CCTGCTCAGTCTTTGACTGGGCTATTCTTGGTTCTGAAGAGAGAGAGACAAGAAG
AGTACATTGAAGAGAAGAAGAGAGTGGACATTGTCGGAAACTCTAACATATGCCCAT
TCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAATAGAACAAATCCTAAAGGAAGA
TCCAGCAAATACGGTTACTCCACTGTGGAAATACCGAAAAAGATGGAAAATCCCCACTCAC
TGCTCACGATGCCAGACACACCAAGGCTATTGCCTATGAGAATGTTATCTAGACAGCAGTG
CACTCCCTAAGTCTGCTCA

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FIGURE 171

MAGSPTCLTLIYILWQLTGSAAAGPVKELGVSGGAVTFPLSKVKQVDSIVWTFNTTPLVT
IQPEGGTIIVTQNRNRERVDFPDGGYSLKLSKLKKNDSGIYYVGIYSSSLQQPSTQEYVLHV
YEHLSKPVMTMGLQSNKNGTCVTNLTCMEHGEEDVIYTWKALGQAANESHNGSILPISWRW
GESDMTFICVARNPVSRNFSSPILARKLCEGAADDPDSSMVLCLLVLPLLSLFVLGLFLW
FLKRERQEYIEEKKRVDICRETPNICPHSGENTEYDTIPHNTRILKEDPANTVYSTVEIP
KKMENPHSLLTMPDTPRLFAYENVI

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FIGURE 172

CTGGTTCCCCAACATGCCTCACCCCATCTATATCCTTGGCAGCTCACAGGGTCAGCAGCC
TCTGGACCCGTGAAAGAGCTGGTCGGTCCGGTGGTGGGCCGTGACTTCCCTGAAGTC
CAAAGTAAAGCAAGTTGACTCTATTGTCTGGACCTCAACACAACCCCTTGTCAACCATA
AGCCAGAAGGGGGCACTATCATAGTACCCAAAATCGTAATAGGGAGAGAGTAGACTTCCA
GATGGAGGCTACTCCCTGAAGCTCAGCAAACCTGAAGAAGAATGACTCAGGGATCTACTATGT
GGGGATATACTACAGCTCATCACTCCAGCAGCCCTCCACCCAGGAGTACGTGCTGCATGTCTACG
AGCACCTGTCAAAGCTAAAGTCACCATGGGTCTGCAGAGCAATAAGAATGGCACCTGTGTG
ACCAATCTGACATGCTGCATGGAACATGGGAAGAGGGATGTGATTATACCTGGAAGGCCCT
GGGCAGCCAATGAGTCCATAATGGGTCCATCCTCCCCATCTCCTGGAGATGGGAG
AAAGTGATATGACCTTCATCTGCAGGAAAGCTGTGAAGGGTGTGCTGATGACCCAGATTCCCTCATGGTCCTCCT
GTGTCCTGTTGGTGCCCTCCTGCTCAGTCTTTGTACTGGGCTATTCTTGGTTTC
TGAAGAGAGAGAGACAAGAAGAGTACATTGAAGAGAAGAAGAGAGTAGGACATTGTCGGAA
ACTCCTAACATATGCCCTCATTCTGGAGAGAACACAGAGTACGACACAATCCCTCACACTAA
TAGAACAACTCTAAAGGAAGATCCAGCAAATACGGTTACTCCACTGTGGAAATACCGAAAA
AGATGGAAAATCCCCACTCACTGCTCACGATGCCAGACACACCAAGGCTATTGCCTATGAG
AATGTTATCTAGACAGCAGTGCACCTCCCTAAGTCTGTGCTCAAAAAAAAAAAAAAAA

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FIGURE 173

GAAAGACGTGGCCTGACAGACAGACAATCCTATTCCCTACCAAAATGAAGATGCTGCTGCT
GCTGTGTTGGACTGACCTAGTCTGTCCATGCAGAAGAAGCTAGTTCTACGGGAAGGA
ACTTTAATGTAGAAAAGATTAATGGGAATGGCATACTATTATCCTGGCCTGTGACAAAAGA
GAAAAGATAGAAGAACATGGCAACTTAGACTTTCTGGAGCAAATCCATGTCTGGAGAA
TTCCTTAGTTCTTAAAGTCCATACTGTAAGAGATGAAGAGTGCTCCGAATTATCTATGGTG
CTGACAAAACAGAAAAGGCTGGTGAATATTCTGTGACGTATGATGGATTCAATACATTACT
ATACCTAAGACAGACTATGATAACTTCTTATGGCTCACCTCATTAACGAAAAGGATGGGA
AACCTTCCAGCTGATGGGCTCTATGCCGAGAACAGATTGAGTTCAGACATCAAGGAAA
GGTTTGCACAACTATGTGAGGAGCATGGAATCCTAGAGAAAATCATTGACCTATCCAAT
GCCAATCGCTGCCTCCAGGCCGAGAATGAAGAATGCCCTGAGCCTCCAGTGTGAGTGGAC
ACTTCTCACCAGGACTCCACCATCATCCCTCCTATCCATACAGCATCCCCAGTATAAATC
TGTGATCTGCATTCCATCCTGTCTCACTGAGAAGTCCAATTCCAGTCTATCAACATGTTACC
TAGGATACCTCATCAAGAATCAAAGACTTCTTAAATTCTCTTGTACACCCCTGACAAT
TTTCATGAAATTATTCCCTCTCCTGTTCAATAATGATTACCCCTGCACTTAA

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FIGURE 174

MKMLLLCLGLTLVCVHAEVASSTGRNFNVEKINGEWTIILASDKREKIEEHGNFRLFLEQ
IHVLENSLVLKVHTVRDEECSELSMVADKTEKAGEYSVTYDGFNTFTIPKTDYDNFLMAHLI
NEKDGETFQLMGLYGREPDLSSEDIKERFAQLCEEHGILRENIIDLDSNANRCLQARE

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FIGURE 175

GGCTCGAGCGTTCTGAGCCAGGGTGACCATGACCTGCTGCGAAGGATGGACATCCTGCAA
TGGATTCAGCCCTGCTGGTTCTACTGCTGTTAGGAGTAGTTCTCAATGCGATACCCTCTAATTG
TCAGCTTAGTTGAGGAAGACCAATTCTCAAAACCCATCTCTGCTTGAGTGGTGGTTC
CCAGGAATTATAGGAGCAGGTCTGATGCCATTCCAGCAACAACAATGTCCTTGACAGCAAG
AAAAAGAGCGTGCTGCAACAACAACAGAACTGGAATGTTCTTCATCATTTCAGTGTGATCA
CAGTCATTGGTGCTCTGTATTGCATGCTGATATCCATCCAGGCTCTTAAAGGTCTCTC
ATGTGTAATTCTCAAGCAACAGTAATGCCAATTGTAATTTCATTGAAAAACATCAGTGA
CATTCATCCAGAACCTCAACTTGCAGAGTGGTTTCATGACTCTGTGCACCTCCTACTG
GTTCAATAAACCCACCAGTAACGACACCATGGCGAGTGGCTGGAGAGCATCTAGTTCCAC
TTCGATTCTGAAGAAAACAAACATAGGCTTATCCACTCTCAGTATTAGGTCTATTGCT
TGTGGAATTCTGGAGGTCTGTTGGGCTCAGTCAGATAGTCATCGGTTCTGGCTGTC
TGTGTGGAGTCTCAAGCGAAGAAGTCAAATTGTGTTAATGGGAATAAAATGTAAGTA
TCAGTAGTTGAAAAA

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FIGURE 176

MTCCEGWTSCNGFSLLVLLLGVVVLNAIPLIVSLVEEDQFSQNPISCFEWWFPGIIGAGLMA
IPATTMSLTARKRACCNRTGMFLSSFFSVITVIGALYCMLISIQALLKGPLMCNSPSNSNA
NCEFSLKNISDIHPESFNLQWFFNDSCAPPTGFNKPTSNDTMASGWRASSHFHFDSEENKHRL
IHFSVFLGLLLGVGILEVLFGLSQIVIGFLGCLCGVSKRRSQIV

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FIGURE 177

GTCGAATCAAATCACTCATTGTGAAAGCTGAGCTCACAGCCGAATAAGCCACCATGAGGCT
GTCAGTGTGTCTCCTGATGGTCTCGCTGCCCTTGCTGCTACCAGGCCATGCTCTGTCT
GCCAGCTGTTGCTCTGAGATCACAGTCTTATTCTTAAGTGACGCTGCGGTAAACCTC
CAAGTTGCCAAACTTAATCCACCTCCAGAAGCTCTGCAGCCAAGTTGGAAGTGAAGCACTG
CACCGATCAGATATCTTTAAGAACGACTCTCATTGAAAAAGTCCTGGTGGAAATGTGAA
AAAATGTGGTGTGTGACATGTAAAATGCTAACCTGGTTCCAAAGTCTTCAACGACACC
CTGATCTTCACTAAAAATTGTAAAGGTTCAACACGTTGCTTAATAAATCACTGCCCTGC

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FIGURE 178

MRLSVCLLMVSLALCCYQAHALVCPAVASEITVFLFLSDAAVNLQVAKLNPPPEALAAKLEV
KHCTDQISFKKRLSLKKSWWK

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FIGURE 179

ATCCGTTCTCTGCGCTGCCAGCTCAGGTGAGCCCTGCCAAGGTGACCTCGCAGGACACTGG
TGAAGGAGCAGTGAGGAACCTGCAGAGTCACACAGTTGCTGACCAATTGAGCTGTGAGCCTG
GAGCAGATCCGTGGGCTGCAGACCCCCGCCAGTGCCTCTCCCCCTGCAGCCCTGCCCTC
GAACTGTGACATGGGAGAGAGTGACCCCTGCCCTTCCTACTGGCAGGCCTGACTGCCTGG
AAGCCAATGACCCATTGCCAATAAAGACGATCCCTCTACTATGACTGGAAAAACCTGCAG
CTGAGCGGACTGATCTGCGGAGGGCTCCTGGCATTGCTGGGATCGCGGAGTTCTGAGTGG
CAAATGCAAATAAGAGCAGCCAGAAGCAGCACAGTCCGTACCTGAGAAGGCCATCCCAC
TCATCACTCCAGGCTGCCACTACTTGCTTGAGCACAGGACTGCCCTCCAGGGATGCCCTGA
AGCCTAACACTGGCCCCCAGCACCTCCTCCCTGGGAGGCCTTATCCTCAAGGAAGGACTTC
TCTCCAAGGCAGGCTGTTAGGCCCTTCTGATCAGGAGGTTCTTATGAATTAAACTCG
CCCCACCACCCCTCA

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FIGURE 180

MERVTLALLLAGLTALEANDPFANKDDPFYYDWKNLQLSGLICGGLAIAGIAAVLSGKCK
YKSSQKQHSPVPEKAIPLITPGSATTC

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FIGURE 181

GGAGAAGAGGTTGTGGGACAAGCTGCTCCGACAGAAGGATGTCGCTGCTGAGCCTGCC
TGGCTGGGCCTCAGACCGGTGGCAATGTCCCCATGGCTACTCCTGCTGCTGGTTGTGGCTC
CTGGCTACTCGCCCGCATCCTGGCTGGACCTATGCCTCTATAACAACACTGCCGCCGGCTCC
AGTGTTCACAGCCCCAAAACGGAACGGTTTGGGTACCTGGCCTGATCACTCCT
ACAGAGGAGGGCTTGAAGGACTCGACCCAGATGTCGCCACCTATTCCAGGGCTTACGGT
ATGGCTGGTCCCACATCCCCTCATCGTTTATGCCACCTGACACCATCCGGTCTATCA
CCAATGCCTCAGCTGCCATTGCACCCAGGATAATCTTCATCAGGTCCTGAAGCCCTGG
CTGGGAGAAGGGATACTGCTGAGTGGCGGTGACAAGTGGAGCCACCCTGGATGCTGAC
GCCGCCTCCATTCAACATCCTGAAGTCCTATATAACGATCTTCAACAAGAGTGCAAACA
TCATGCTTGACAAGTGGCAGCACCTGGCTCAGAGGGCAGCAGTCGTCTGGACATGTTGAG
CACATCAGCCTCATGACCTTGGACAGTCTACAGAAATGCATCTTCAGCTTGACAGCCATTG
TCAGGAGAGGCCAGTGAATATATTGCCACCATTTGGAGCTCAGTGCCTGTAGAGAAAA
GAAGCCAGCATATCCTCCAGCACATGGACTTCTGTATTACCTCTCCATGACGGCGGCG
TTCCACAGGGCCTGCCGCTGGCATGACTTCACAGACGCTGTATCCGGAGCGCGTCTG
CACCCCTCCCCACTCAGGGTATTGATGATTTTCAAAGACAAAGCCAAGTCCAAGACTTGG
ATTTCATTGATGTGCTTCTGCTGAGCAAGGATGAAGATGGGAAGGCATTGTCAGATGAGGAT
ATAAGAGCAGAGGCTGACACCTCATGTTGGAGGCCATGACACCACGGCCAGTGGCTCTC
CTGGGTCTGTACAACCTTGCAGGCACCCAGAATACCAGGAGCGCTGCCACAGGAGGTGC
AAGAGCTTCTGAAGGACCGCGATCCTAAAGAGATTGAATGGGACGACCTGGCCAGCTGCC
TTCCCTGACCATGTGCGTGAAGGAGAGCCTGAGGTTACATCCCCCAGCTCCCTCATCTCCG
ATGCTGCACCCAGGACATTGTTCTCCAGATGGCCAGTCATCCCCAAAGGCATTACCTGCC
TCATCGATATTATAGGGTCCATCACAAACCAACTGTGTGGCCGGATCCTGAGGTCTACGAC
CCCTTCCGCTTGACCCAGAGAACAGCAAGGGAGGTACCTCTGGCTTTATTCTTCTC
CGCAGGGCCCAGGAACGTGATCGGCAGGCAGTCGCATGGGGAGATGAAAGTGGCTCTGG
CGTTGATGCTGCTGCACTCCGGTTCTGCCAGACCAACTGAGCCCCCAGGAAGCTGGAA
TTGATCATGCGCGCCGAGGGCGGGCTTGGCTGCAGGCTGAATGTAGGCTTGCA
GTGACTTCTGACCCATCCACCTGTTTGCAGATTGTCATGAATAAACGGTGCTGTCAA

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FIGURE 182

MSLLSLPWGLRPVAMSPWLLLLLVGSWLLARILAWTYAFYNNCRRLQCFPQPKRNWFWG
HLGLITPTEEGLKDKSTQMSATYSQGFTVWLGPPIIPFIVLCHPDTIRSITNASAAIAPKDNLF
IRFLKPWLGEGLGGDKWSRHRMLTPAFHFNILKSYITIFNKSANIMLDKWQHLASEGS
SRLDMEHISLMTLDSLQKCIFSFDSHCQERPSEYIATILELSALVEKRSQHILQHMDFLYY
LSHDGRRFHACRLVHDFTDAVIRERRRLPTQGIDDDFKDKAKSKTLDFIDVLLLSKDEDG
KALSDEDIRAEADTFMFGGHDTTASGLSWVLYNLRHPEYQERCRCQEVQELLKDRDPKEIEW
DDLAQLPFLTMCVKESRLHPPAPFISRCCTQDIVLPDGRVIPKGITCLIDIIGVHHNPTVW
PDPEVYDPFRFDPENSKGRSPLAFIPFSAGPRNCIGQAFAMAEMKVVLALMLLHFRFLPDHT
EPRRKLELIMRAEGGLWLRVEPLNVGLQ

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FIGURE 183

CAACAGAAGCCAAGAAGGAAGCCGTCTATCTTGTGGCGATC**ATGT**TATAAGCTGGCCTCCTGC
TGTTTGCTTTCACAGGATTCTTAAATCCTCTTATCTCTCCCTCTCCTTGACTCCAGGGA
AATATCCTTCAACTCTCAGCACCTCATGAAGACGCGCGCTTAACCCGGAGGAGCTAGAAA
GAGCTTCCCTCTACAGATATTGCCAGAGATGCTGGGTGCAGAAAGAGGGGATATTCTCAGG
AAAGCAGACTCAAGTACCAACATTTAACCCAGAGGAAATTGAGAAAGTTCAAGGATT
CTCTGGACAAGATCCTAACATTACTGAGTCATCTTGGCCAGAACATGGAAACCATA
AGAAACGTGAGACTCCTGATTGCTCTGGAAACTGTGTCT**TGA**AGTGAATAAGCATCTGT
TAGTCAGCTCAGAACACCCATCTAGAATATGAAAAATAACACAATGCTTGATTGAAAAC
AGTGTGGAGAAAAACTAGGCAAACACACCCCTGTTCATTTGTTACCTGGAAAATAATCCTCT
ATGTTTGACAAAAAAAAAAAAAA

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FIGURE 184

MYKLASCCLLFTGFLNPLSLPLLDREISFQLSAPHEDARLTPEELERASLLQILPEMLGA
ERGDILRKADSSTNIFNPRGNLRKFQDFSGQDPNILLSHLLARIWKPYKKRETPDCFWKYCV

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FIGURE 185

GAACATTTAGTCCAAAGGAATGTACATCAGCCCCACGGAAGCTAGGCCACCTCTGGAT
GGGGTTGCTGGTTAAAACAAACGCCAGTCATCCTATATAAGGACCTGACAGCCACCAGGCA
CCACCTCCGCCAGGAACTGCAGGCCACCTGTCTGCAACCCAGCTGAGGCCATGCCCTCCCC
AGGGACCGTCTGCAGCCTCCTGCTCTGGCATGCTCTGGCTGGACTTGGCATGGCAGGCT
CCAGCTTCCTGAGCCCTGAACACCCAGAGAGTCAGCAGAGAAAGGAGTCGAAGAAGCCACCA
GCCAAGCTGCAGCCCCGAGCTCTAGCAGGCTGGCTCCGCCGGAAAGATGGAGGTCAAGCAGA
AGGGGCAGAGGATGAACTGGAAGTCCGGTTAACGCCCTTGATGTTGGAATCAAGCTGT
CAGGGGTTCACTTACGAGCAGCACAGCCAGGCCCTGGGAAGTTCTTCAGGACATCCTCTGG
GAAGAGGCCAAAGAGGCCAGCCGACAAGTGATCGCCACAAGCCTACTCACCTCTCT
AAGTTAGAAGCGCTCATCTGGCTTTCGCTTGCTGCAGCAACTCCCACGACTGTTGTA
CAAGCTCAGGAGGCCAATAATGTTCAAACGTGA

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FIGURE 186

MPSPGTVCSLLLLGMLWLDLAMAGSSFLSPEHQRVQQRKESKKPPAKLQPRALAGWLRPEDG
GQAEGAEDELEVRFNAPFDVGIKLSGVQYQQHSQALGKFLQDILWEEAKEAPADKO

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FIGURE 187

CGGCCACAGCTGGCATGCTCTGCCATGCCATCCTGCTGTATGTCCTCGTCCAGTACCTC
GTGAACCCCCGGGGTGCCTCCGCACGGACCCCAGATGTCAGAAATTGAACACGTGGCTGCTGT
TCCTCCCCCTGTTCCCGGTGCAGGTGCAGACCCCTGATAGTCGTGATCATGGGATGCTCGTG
CTCCTGCTGGACTTCTGGCTGGTGCACCTGGGCCAGCTGCTCATCTCCACATCTACCT
GAGTATGTCCCCCACCCCTAACGCCCCGATCCCCCAAGGCTGGGTGGTCAGAGCTGCTCATC
TTACACCTCTACTTGAGTATGTCCTAACCCCTGAGCCCCCACGCCTGGGCCAGAGTCTTT
GTCCCCCGTGTGCGCATGTTCAAGGTCAGCCTCTCCAGAAAGTGAGATCATGGACAAAAA
GGCAAATCACAGGAAGAAATTAAATCCATGAGGACCCAGCAGGCCAGCAAGAAGCTGAAC
TCACGCCGAGACCTGCAGGAGTGGTGCAGGTGCTTGAAGTAACAAGTTAAAATGTTAGA
GACAATGGAATGGAATCTATTAGGCAAGAACAGGACATTATGAAATAAGGACAGGTGGACTT
CCAAAAACACAAGTAGAAATTCTAACAAATGAAATATATTACAGGCAGGTACCCACTAACCA
AACAACTGAAGCGAGAGCTGTGGTCTTGCTGGTCACAGTGGCACAGCGGTAGGCAGGTC
AGTCATGTTGCTGAACGACGGAGGGTAAACTCCCCAGCCCCAAGAAAACCTGTGTTGGAAGT
AACAAACAACCTCCCTGCTCCTGGCACCCAGCCGTTGGTCATGGTGGGCCAGCTGCAAAGCG
TCTTCCATTCTCTGGCAGTGGTGGCCAGGCTGTGGCCTCTCAGGGGTTCTGTGGAC
ACGGGCAGCAGAGTGTCCAGGCCAGCCCCAAGAATGCCCTGCTCCTGACAGCTTGGCCA
ACCCCTGGTCAGGGCAGAGGGAGTTGGTGGTCAGGCTCTGGCTCACCTCCATCTCCAGA
GCATCCCTGCTGCAGTTGTGCAAGAACGCCCCAGCTCAGAAATGAACACACCCACCAAGA
GCCTCCTGTTCATAACACACAGGTTACCCCTACAAACCAACTGTCCCCACACAACCCCTGGGAT
GTTTAAAACACACACCTCTAACGCATATCTTACAGTCAGTGTGCTTGCTGAGGGTTGA
ATTTTTTTAATGAAAGTGCATGAAAATCACTGGATTAAATCCTACGGACACAGAGCTGAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 188

MNTWLLFLPLFPVQVQTLIVVIIGMLVLLDFLGLVHLGQLLIFHIYLSMSPTLSPRSPQGW
VVRAAHLTPLLEYVPNPEPPTPGARVFVPRVRMCSGSASPRSEIMDKKGKSQEEIKSMRTQQ
AQQEAEELTPRPAGVVPGA

FIGURE 189

GGAGTGCAGATGGCATCCTCGTTCTCCAGACAAGCTGCAAGACGCTGACCATGCCAAG
ATGGAGCTCTCGAAGGCCTCTCTGCCAGCGGACACTCCTATCTGCCATCCTCAGCATGCT
ATCACTCAGCTCTCCACAACATCCCTGCTCAGCAACTACTGGTTGTGGGACACAGAAGG
TGCCCAAGCCCCGTGCGAGAAAGGTCTGGCAGCCAAGTGCTTGACATGCCAGTGTCCCTG
GATGGAGATACCAACACATCCACCCAGGAGGTGGTACAATACAACACTGGGAGACTGGGGATGA
CCGGTTCTCCTCCGGAGCTTCCGGAGTGGCATGTGGCTATCCTGTGAGGAAACTGTGGAAG
AACCAAGGGAGAGGTGCCGAAGTTTATTGAACTTACACCACCAGCCAAGAGAGGTGAGAAA
GGACTACTGGAATTGCCACGTTGCAAGGCCATGTCACCCACTCTCGATTGGAGGGAA
GCGGTTGATGGAGAAGGCTTCCCTCCCTCCCTGGGCTTGTGGCAAAAATCCTA
TGGTTATCCCTGGGAACGCAGATCACCTACATCGGACTTCAATTCATCAGCTTCCCTGCT
ACTAACAGACTGCTACTCACTGGAACCCCTGCCTGTGGCTCAAACGTAGCGCCTTGCTG
CTGTTTCCCTGTCCTGTCAGGTCTCCTGGGATGGTGGCCACATGATGTATTCAAGTC
TTCCAAGCGACTGTCAACTTGGTCCAGAAGACTGGAGACCACATGTTGAATTATGGCTG
GGCCTCTACATGGCCTGGCTCTCCTCACCTGCTGCATGGCGTCGGCTGTCAACCACCTCA
ACACGTACACCAGGATGGTGGAGTTCAAGTGCAAGCATAGTAAGAGCTCAAGGAAAAC
CCGAACGTGCTTACCATCACCATCAGTGTTCCTCGGCGCTGTCAAGTGCAAGCCCCAC
CGTGGGTCTTGACCAGCTACCACCGATCATAAATCAGCCCACACTCTGTCTTGAGG
GAGTCGACTTCACTCCGAGCTGCGAACAGGGATTCAAAGAGGGGCCAGCCAGGAGCTG
AAAGAAGCAGTTAGGTCACTGTAGAGGAAGAGCAGTGTAGGAGTTAACGGGTTGGGA
GTAGGCTTGAGCCCTACCTACACGTCTGCTGATTATCAACATGTGCTTAAGCCAACATCCG
TCTCTTGAGCATGGTTTAGAGGCTACGAATAAGGCTATGAATAAGGGTTATCTTAAAGC
CTAAGGGATTCCCTGGGTGCCACTGCTCTCTTACAGCTCCATCTGTTCACCCAC
CCCACATCTCACACATCCAGAATTCCCTCTTACTGATAGTTCTGTGCCAGGTTCTGGC
TAAACCATGGAGATAAAAGAAGAGTAAACACTTCCGACCTTAAGGATCTGAAA

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FIGURE 190

MAKMELSKAFSGQRTILLSAILSMLSLSFSTTSLLSNYWFVGTQKVPKPLCEKGIAAKCFDMP
VSLDGDTNTSTQEVVQYNWETGDDRFSFRSFRSGMWLSCEETVEEPGERCRSFIELTPPAKR
GEKGLLEFATLQGPCHPTLRFGGKRLMEKASLPSPPLGLCGKNPMVIPGNADHLHRTSIHQL
PPATNRLATHWEPCWLWAQTERLCCCFLCPVRSPGDGGPHDVFTSLPSDCQLGSRRLETTCLE
LWLGLLHGLALLHLLHGVGCHHLQHVHQDGAGVQVQA

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FIGURE 191

AACTGGAAGGAAAGAAAGAAAGGTAGCTTGGCCCAGATGTGGTTACCCCTGGTCTCCTG
TCTTTATGTCTTCTCCTCTTCTATTCTGTATCTCCCTCACTTAAGTCTCAGGCCTGTCA
GCAGCTCCTGTGGACATTGCCATCCCTCTGGTAGCCTCAGAGCAAACAGGACAACCTATG
TTATGGATGTTCCACCAACCAGGGTAGTGGCATGGAGCACCGTAACCATCTGTGCTCTGT
GATCTCTATGACAGAGGCCACTTCTCCACCTCTGAAATGTTCCCTGCTCTGAAATCTGGCATG
AGATGGCACAGGTGACCACGCAGAAGCCACCAGAAATCTGCCTGCCCTATTCCCTCCCAA
GTCTGTTCTTATTGTCAACCTCAGCACAAACAGGCTGGGCCAATGGCATTACAGAGAAAG
CAATCTGTGGCTAGTGGCAGATTACCATGCAAGCCCCAGGAGAAATGGAGGAGCTTGT
AGCCACCTCCCTGTCAGCCAGTATTAACATGTCCCCTCCCCCTGCCCGCCGTAGATTCA
GACATTGCCCTGTGTGCCACCAAACCAGGACTTCCCTGGCTGGCATCCCTGGCTCT
CTCCTGGTACCCAGCAAGACGTCTGTTCCAGGGCAGTGTAGCATTTCAAGCTCCGTTACT
ATGGCGATGCCATGATGTTACAATCCCACCTGCCTGAATAATCAAGTGGAAAGGGAAAGCA
GAGGGAAATGGGCCATGTGAATGCAGCTGCTGTCTCCCTACCTGAGGAAAAACCAA
GGGAAGCAACAGGAACCTCTGCAACTGGTTTATCGGAAAGATCATCCTGCCTGCAGATGC
TGTTGAAGGGCACAAGAAATGTAGCTGGAGAAGATTGATGAAAGTGCAGGTGTGAAGGAA
ATAGAACAGTCTGCTGGAGTCAGACCTGGATTCTGATTCCAAACTCTTATTACTTGG
AAGTCACTCAGCCTCCCCGTAGCCATCTCCAGGGTGACGGAACCCAGTGTATTACCTGCTGG
AACCAAGGAAACTAACAAATGTAGGTTACTAGTGAATACCCCAATGGTTCTCCAATTATGCC
CATGCCACCAAAACAATAAAACAAAATTCTCTAACACTGAAA

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FIGURE 192

MWLPLGLLSLCLSPLPILSSPSLKSQACQQLLWTLPSPPLVAFRANRTTYVMDVSTNQGSGME
HRNHLCFCDCLYDRATSPPLKCSLL

FIGURE 193

GTAGCGCGTCTGGGTCTCCGGCTGCCGCTGCTGCCGCCGCCCTGGGTCTGGAGGCCAGGAGCGACGTCA
CCGCCATGGCAGGCATCAAAGCTTGTATTAGTTGCTTGGAGGAGCAATCGGACTGATGTTTGATGCTT
GGATGTGCCCTCCAATATAACAACAAATACTGGCCCTCTTGTCTATTTTACATCCTTCACCTATTCC
ATACTGCATAGCAAGAAGATTAGTGGATGATACAGATGCTATGAGTAACGCTTGTAAAGGAACITGCCATCTTC
TTACAACGGGCATTGTCGTGTCAGCTTGGACTCCCTATTGTATTGCAAGCAGCACATCTGATTGAGTGGGAAG
GCTTGTGCACTGTTCTCACAGGAAACACAGTCATCTTGCAACTATACTAGGCTTTCTTGGTCTTGGGAAG
CAATGACGACTTCAGCTGGCAGCTGGTGAAGAAGAAATTACTGAACATTGTCAAATGGACTTCCGTGTCATT
GTTGGCCATTCAACGCACACAGGAGATGGGAGCTTAATGCTGAATGGTATAGCAAGCCTCTGGGGTATT
GGTGCCTCCCTCTCACTTTATTGTAAAGCATACTATTTACAGAGACTGCTGAAGGATAAAAGGATTTCT
CTTTGGAAAGCTTGACTGATTTCACACTATCTATAGTATGCTTTGTGGTCTGCTGAATTAAATAT
TTATGTGTTTCCTGTTAGGTTGATTTTTGAAATCAATATGCAATGTTAACACTTTTTAATGTAATCA
TTTGCATTGGTAGGAATTCAAGAATTCGCCGGCTCTATTACTGGTCAAGTACATCTTCTTAAATTATT
TAGCCTCCATTATTACAAAAAAATTATAAAAGTTTCAGTCAGTCAGGATGACATCACTCCCAATGTTATG
CAGACATACAGACGGTGGCATACTGTTAGACTGTACTCAGTGCACATTACCTCAGAG
GGGCCAAGTGTAAATGCCATGCCCTCCGTTAAGGGTTGTTACTGGTAGACAGATGTTTGTGGATG
AAAATTATTATGGAATTGCTACAGAGGAGTGCTTTCTTCAATTGTTAGAAGAATTATGTTAAACTTA
AGGTAAAGGGTGTAAAACATTGAGATAAGGTTTATTATGTTATTGTTAGAGTGAGTTGCAATG
GGGAAGAAATGACATTGAAATTCCAGTTTGAAATCCTGTTCTATTATAAGTGAATTGATCTCCTATC
AACCTTCATGTTTACCTGTTAAAGGACATACATGGAACCAACTGATGAGGGACAGTTGATGTTG
ATCATATATGCAAGAAAACCTCCTGCTCCCTTTGACTTATTGGTATGTTGATATATTACATAAAA
TAACTTTCAAATATAGTTAATAACACTTAGAAGTGTACTTACCTGAAAATAATTGCTATGCCGTACATT
CAGAGTGCCCTCCCTGCAAGGCCTGCCATGATTAACAAGTAACTTGTAGTCTACAGATAATTGCA
TTAACAGTTAAGATTAGACCATGGTAATAGTAGTTCTTATTCTAAGGTTATATCATATGTAATTAAAG
TATTTTAAGACAAGTTCCGTATAACCTCTGAACTGTTGATTTGAGTTCATCATGATAGATCTGCTGTT
CCTTATAAAAGCATTGTTGAGTTAATGCAAAGTAGCCAAGTCCAGCTATAGCAGCTTCAGAAACAT
ACCTGACCAAAAAATTCCAGTAACCAAGGAGTCATGCAATTATAGTGGCTGTTACATCTAATAATTACAGGA
CTTTTCAGGAGTGGGTTAAAAACATTGCAAGTTGGTCTGACAGTATTGTTAAGGATATTGTTGATG
TTTATTGAGTTATTCTCAAGAAAATGGAATAATTGGGATTGTCAGCTTTACTAAAGATGCCCTAA
AGCCACAGGTTTATTGCCCTAAGCCATGACTTTAGATATGAGATGACGGGAAGCAGGAGCAAATATCG
GCGTGTGGCTGGAGCCTCCACTGGAGGCTGAAAGTGGCTGTTAGTATAATGTCAGATTCAAGAGGAA
GGTGCAGGTACACATGAGTTAGAGAGCTGGTGAGACAGTTGGGAACTTTGCTGCTGATCTACTGGACTT
TTTTTGCAAGGAAGTGCATTCTGTCCTCCCTATTCTGTTGGATGTCAGTGCAGTGCACTGCTACTG
TTTATCCACTGGCCACAGACTTTCTAACAGCTGCGTATTATTCTATATACTAATTGCAATTGGCAGCATT
GTGTCCTTGACCTTGATAGCTGACATAGTGTCTGATTTCTAGGCTAGTTACTTGAGATATGAAT
TTCCATAGAATATGCACTGATAACACATTACCATCTTCTATGGAAAGAAAATTGATGATGAAACAATAA
AGAATTAAATATCTATTAAAAAA

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FIGURE 194

MAGIKALISLSFGGAIGLMFLMLGCALPIYNKYWPLFVLFFYILSPIPYCIARRLVDDTDAM
SNACKELAIFLTTGIVVSAFGLPIVFARAHLIEWGACALVLTGNTVIFATILGFFLVFGSND
DFSWQQW

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FIGURE 195

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FIGURE 196

MDFLLLGLCLYWLLRRPSGVVLCLLGACFQMLPAAPSGCPQLCRCEGRLLYCEALNLTEAPH
NLSGLLGLSLRYNSLSELRAGQFTGLMQLTWLYLDHNNHICSVQGDAFQKLRRVKELTLSNQ
ITQLPNTTFRPMPNLRSDVLSYNKLQALAPDLFHGLRKLTTLHMRANAIQFVPVRIFQDCRS
LKFLDIGYNQLKSLARNASFAGLFKLTELHLEHNDLVKVNFAHFPRILISLHSLCLRRNKVAIV
VSSLDWVNLEKMDLSGNEIEYMEPHVFETVPHLQLQLDSNRLTYIEPRILNSWKSLTSIT
LAGNLWDCGRNVCALASWLSNFQGRYDGNLQCASPEYAQGEDVLDAVYAFHLCEDGAEPTSG
HLLSAVTNRSDLGPPASSATTLAGGEGQHDGTFEPATVALPGGEHAENAVQIHKVVTGTMA
LIFSFLIVVLVLYVSWKCFPASLRQLRQCFVTQRRKQKQKQTMHQMAAMSAQEYYVDYKPNH
IEGALVIINEYGSCTCHQQPARECEV

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FIGURE 197

GTGCAAGGAGCCGAGGCGAGATGGCGTCTGGCCGGTCTGCTGGCTGCAGCTCTGC
GCACTGACCCAGGCGGTCTCAAACCTCTGGTCCCCAACACGGACTTCGACGTGCAGCAA
CTGGAGCCAGAACCGGACCCGTGCGCCGGCGGCCGTTGAGTCCCGGGACAAGATGG
TGTCAAGTCTGGTGCAAGAAGGTACGCCGTCTCAGACATGCTCCTGCCGCTGGATGGGAA
CTCGTCTGGCTTCAGGAGCCGGATTGGCGTCTCAGACGTGGCTCGCACCTGGACTGTGG
CGCGGGCGAACCTGCCGTCTCCGCGACTCTGACCGTTCTCCTGGCATGACCCGACCTGT
GGCGCTCTGGGACGAGGCACCTGGCCTTTCTCGTGGACGCCGAGCGCGTGCCTGCCGC
CACGACGACGTCTTCTTCCGCCTAGTGCCTCCTCCCGTGGCTCGCCCTGGCGCTAG
CCCCGTGCGTGTCCGCAGCATCTCGGCTCTGGCCGGACGTTCACGCGCAGGAGGACCTGG
CTGTTTCCTGGCGTCCCGCGGGCCGCTACGCTTCCACGGGCCGGCGCTGACGTGC
GGCCCCGAGGACTGCGCGGACCCGTGGCTCGTCTGCCAACGCCGAGGCGCAGCCGTG
GATCTGCGCGGCCCTGCTCCAGCCCCCT

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FIGURE 198

MGVLGRVLLWLQLCALTQAVSKLWVPNTDFDVAANWSQNRTPCAGGAVEFPADKMVSVLVQE
GHAVSDMLLPLDGEVLASGAGFGVSDVGSHLDCGAGEPAVFRDSDRFSWHDPHLWRSGDEA
PGLFFVDAERVPCRHDDVFFPPSASFRVGLGPASPVRVRSISALGRTFTRDEDLAVFLASR
AGRLRFHGPAGALSGPVEDCADPSGCVCGNAAQPWICAALLQP

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FIGURE 199

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FIGURE 200

MGPVKQLKRMFEPTRLIATIMVLLCFALTLCASFWWHNKGALIFCILQSLALTWYSLSFIP
FARDAVKKCFAVCLA

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FIGURE 201

TTGAGCGCAGGTGAGCTCCTGCGCTTCCGGGGCGTTCCTCCAGTCACCCCTCCGCCGTTACCCGCCGGCG
CCGAGGGAGTCCTCCAGACCCCTCCCTCCGTCCTCAAACATAATACGGACTGAACGGATCGCTGCCAGGGT
GGGAGAGAAAATTAGGGGGAGAAAGGACAGAGAGAGCAACTACCATCCATAGCCAGATAGATTATCTTACACTG
AACTGATCAAGTACTTTGAAAATGACTTCGAAATTATCTGGTGTCTCATACTTGCTGACTGAGTCTTC
AACACCTTTCTCTCCAACTAGACCAAGAGGTTCTACTAGTTCTTGATGGATTCCGTGGGATTACT
TATATAAAGTCCAACGCCCATTTCAATTATATTGAAATATGGTGTACGTGAAGCAAGTACTAATGTT
TTTATTACAAAACCTACCCATAACCAATTACTTGGTAACGGCCTTTGCAGAGAATCATGGGATTGTTGC
AAATGATATGTTGATCCTATTGGAACAAATCTTCTCTGGATCACATGAATATTATGATCCAAGT
GGGAAGAAGCGACACCAATATGGATCACAAACAGAGGGCAGGACATACTAGTGGTGCAGCCATGTGGCCGGA
ACAGATGTAACATAAGCGCTTCCACTCATTACATGCCCTACAATGAGTCAGTTCAATTGAAGATAG
AGTGCACAAATTGTTGAACTGGTTACGTCAAAAGAGCCATAAAATCTGGTCTTCTATTGGGAAGACCC
ATGACATGGGCCACCATTTGGGACCTGACAGTCGCTCATGGGCCTGTCATTTCAGATATTGACAAGAAGTTA
GGATATCTCATACAAATGCTGAAAAGGCAAAGTGTGGAAACACTCTGAACCTAATCATCACAGTGT
AATGACGCACTGCTCTGAGGAAAGGTTAATAGAAGACTGACAGTACCTGGATAAAAGGACACTATACCTG
ATCAATCTCCAGTAGCAGCCATCTGGGAAAAGGTTAATTTGATGAAGTCTATGAAGCACTAAC
CATCCTAATCTACTGTTACAAAAAGAACGCTTCCAGAAAGGTGGCATTACAAATACAACAGTCGAATTCA
ACCAATCATAGCAGTGGCTGATGAAGGGTGGCACATTACAGAATAAGTCAGATGACTTCTGTTAGGCAACC
ACGGTTACGATAATGCGTTAGCAGATATGCATCCAATTTAGCCATGGTCTGCCCTCAGAAAGAATT
TCAAAAGAAGCCATGAACCTCACAGATTGTAACCAACTATGCCACCTCCCAATATCACTGCCATGCCACA
CAATGGATCATCTGGAATGTCCAGGATCTGCTCAATTGCAATGCCAAGGGTGGCCCTTACACAGAGTA
CTATACTCCTCCCTGGTAGTGTAAACCAGCAGAATATGACCAAGAGGGTCATACCCATTATTCATAGGGTC
TCTCTGGCAGCATTAGTGTATTGTAATTTCATTAAGCATTAAATTCAAGTCAAATAC
CTTACAAGATATGCATGCTGAAATGCTCAACCATTACAAGCCTAATGTTACTTGAAGTGATTTGCATA
TTGAAGTGGAGATTCCATAATTATGTCAGTGTAAAGGTTCAAATTCTGGGAACACAGTTCCAAACATCTGC
AGAAACCATTAAGCAGTTACATATTAGGTATACACACACACACACACACACACACAGGACCAAA
ATACTACACCTGCAAAGGAATAAGATGTGAGAGTATGTCTCCATTGTCAGTGTAGCATAGGGATAGATAAG
ATCTGCTTATTGGACTTGGCAGATAATGTATATTAGCAACTTGCAGTATGAAAGTACCTTAT
ATTGCACTTTAAATTCTCCTGATGGTACTTTAATTGAAATGCACTTTATGGACAGTTATGCTTATAAC
TTGATTGAAAATGACAACCTTTGCACCCATGTCAAGAATACTTGTACGCATTGTCAAACTGAAGGAATT
TCTAATAATCCGAATAATGAACATAGAAATCTATCTCCATAAAATTGAGAGAAGAAGAGGTGATAAGTGTGA
AAATTAAATGTGATAACCTTGAACCTTGAATTGGAGATGTATTCCCAACAGCAGAATGCAACTGTGGCAT
TTCTGTCTATTCTTCCAGAGAACGTTGTTCATTTATTCCCTCAAAAGAGAGTCAGCAACT
ATTGCTTCTAAATATATTGTTCTGTCATAAAATTATTGTGATTCCCTGATGAGTCATATTACTGTGATTTCA
TAATAATGAAGACACCAGAATATACTTTCTTCTATAGTTCAAGCAATGCCCTGAATAGAAGCAACCAGGCA
CCATCTCAGCAATGTTCTTGTAAATTATTGCTCCCTTGAAGAATTAACACTATTAAATTACATTAA
AAATCAAATTGATAAAAAAAAAAAAAAA

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FIGURE 202

MTSKFILVSFILAALSLSTTFSLQLDQQKVLLVSFDGFRWDYLYKVPTPHFHYIMKYGVHVK
QVTNVFITKTYPNHYTLVTGLFAENHGIVANDMFDPIRNKSFSLDHMNIYDSKFWEETPIW
ITNQRAGHTSGAAMWPGBTDVKIHKRFPHTHMPYNESVSFEDRVAKIVEWFTSKEPINLGLLY
WEDPDDMGHHLGPDSPLMGPVISIDKKLGYLIQMLKKAKLWNTLNLIITSDHGMTQCSEER
LIELDQYLDKDHYTLIDQSPVAAILPKEGKFDEVYEALTHAHPNLTVYKKEDVPERWHYKYN
SRIQPIIAVADEGWHILQNKSDDFLLGNHGYDNALADMPIFLAHGPAFRKNFSKEAMNSTD
LYPLLCHLLNITAMPHNGSFWNVQDLLNSAMPRVVPYTQSTILLPGSVKPAEYDQEGSYPYF
IGVSLGSIIIVIVFFVIFIKHLIHSQIPALQDMHAEIAQPLLQA

Signal Peptide:

amino acids 1-22

Transmembrane Domain:

amino acids 429-452

N-glycosylation sites:

amino acids 101-104, 158-161, 292-295, 329-332, 362-365, 369-372, 382-385, 389-392

Somatomedin B Domain:

amino acids 69-85

Sulfatase protein Region:

amino acids 212-241

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FIGURE 203

GGATTTGTGATCCCGATTGCTCCCACGGCGGGACCTTGTAACTGCGGGAGGCCAG
GACAGGCCACCCCTGCGGGCGGGAGGCAGCCGGGTGAGGGAGGTGAAGAAACCAAGACGC
AGAGAGGCCAACGCCCTGCCTGGTCACACAGCCAAAGGAGGCAGAGCCAGAACTCACAA
CCAGATCCAGAGGCCAACAGGGACATGCCACCTGGGACGAAAAGGCAGTCACCCGAGGGCC
AAGGTGGCTCCGCTGAGAGGATGAGCAAGTTCTAAGGCACCTCACGGTCGTGGAGACGA
CTACCATGCCTGGAACATCAACTACAAGAAATGGGAGAATGAAGAGGAGGAGGAGGAGG
AGCAGCCACCACCCACACCAGTCTCAGGCAGGAAGGCAGAGCTGCAGCCCTGACGTTGCC
CCTGCCCTGGCCCCGCACCCAGGGCCCCCTGACTTCAGGGCATGTTGAGGAAACTGTT
CAGCTCCCACAGGTTTCAGGTACATCATCATCTGCTGGTGGTCTGGATGCCCTCTGGTGC
TTGCTGAGCTCATCCTGGACCTGAAGATCATCCAGCCGACAAGAATAACTATGCTGCCATG
GTATTCCACTACATGAGCATCACCATCTGGTCTTTTATGATGGAGATCATCTTAAATT
ATTGTCTTCCGCCTGAGTTCTTCACCACAAGTTGAGATCCTGGATGCCGTCGTGGTGG
TGGTCTCATTCATCCTGGACATTGCTCCTGTTCCAGGAGCACCAGTTGAGGCTCTGGC
CTGCTGATTCTGCTCCGGCTGTGGCGGGTGGCCCGGATCATCAATGGGATTATCATCTCAGT
TAAGACACGTTCAGAACGGCAACTCTTAAGGTTAAAACAGATGAATGTACAATTGGCCGCCA
AGATTCAACACCTTGAGTTCAAGCTGCTCTGAGAACGCCCTGGACTGAGTTGCTGTATC
AACCTGTAAGGAGAACGCTCTCCGGATGGCTATGGGAATGAAAGAATCCGACTTCTACTCT
CACACAGCCACCGTGAAAGTCTGGAGTAAATGTGCTGTGTACAGAACAGAGAGAGAACAG
CAGGCTGGCATGTTCACTGGCTGGTGTACGACAGAACCTGACAGTCAGTCACTGCCAGTTA
TCACCTCAGATTACAAATCACACAGAGCATCTGCCTGTTCAATCACAAGAGAACAAACC
AAAATCTATAAAGATATTCTGAAAATATGACAGAAATTGACAAATAAGCATAAACGTGTA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 204

MATWDEKAVTRRAKVAPAERMSKFLRHFTVVGDDYHAWNINYKKWENEAAAAAEEQPPPTPV
SGEEGRAAAPDVAPAPGPAPRAPLDFRGMLRKLFFSHRFQVIIICLVVLDALLVLAELILDL
KIIQPDKNNAAMVPHYMSITILVFFMMEIIFKLFVFRLLSSFTTSLRSWMPVVVVVSFILDI
VLLFQEHQFEALGLLILLRLWRVARIINGIIISVKTRSERQLLRLKQMNVQLAAKIQHLEFS
CSEKPLD

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FIGURE 205

CGGCTCGAGCTCGAGCCGAATCGGCTCGAGGGGCACTGGAGCACCCAGCAGGCCGCCAACAT
GCTCTGTCTGTGCCTGTACGTGCCGGTCATCGGGGAAGCCCAGACCGAGTCCAGTACTTTG
AGTCGAAGGGGCTCCCTGCCAGCTGAAGTCCATTTCAGTCAGTGTCTTCATCCCCCTCC
CAGGAATTCTCCACCTACCGCCAGTGGAGCAGAAAATTGTACAAGCTGGAGATAAGGACCT
TGATGGCAGCTAGACTTGAAGAATTGTCCATTCTCCAAGATCATGAGAAGAAGCTGA
GGCTGGTGTAAAGATTTGGACAAAAAGAATGATGGACGCATTGACCGCAGGAGATCATG
CAGTCCCTGCCGGACTTGGAGTCAGAATCTGAACAGCAGGGCAGAAAAAATTCTCAAGAG
CATGGATAAAAACGGCACGATGACCATCGACTGGAACGAGTGGAGAGACTACCAACCTCC
ACCCCGTGGAAAACATCCCCGAGATCATCCTACTGGAAGCATTCCACGATTTGATGTG
GGTGAGAATCTAACGGTCCCAGTGGAGTCACAGTGGAGGAGGGCAGACGGGATGTGGT
GAGACACCTGGTGGCAGGGTGGGGCAGGGGCCATCCAGAAACCTGCACGGCCCCCTGG
ACAGGCTCAAGGTGCTCATGCAGGTCCATGCCCTCCCGCAGCAACACATGGGCATCGTTGGT
GGCTTCACTCAGATGATTCAGAGAAGGAGGGGCCAGGTCACTTGGGGCAATGGCATCAA
CGTCCTCAAAATTGCCCGAATCAGCCATCAAATTATGGCTATGAGCAGATCAAGGCC
TTGTTGGTAGTGACCAGGAGACTCTGAGGATTACAGAGAGGTTGTGGCAGGGCTTGGCA
GGGGCCATCGCCCAGAGCAGCATCTACCCAATGGAGGTCTGAAGACCCGGATGGCGCTGCG
GAAGACAGGCCAGTACTCAGGAATGCTGGACTGCGCCAGGAGGATCCTGGCCAGAGAGGGG
TGGCCGCTTCTACAAAGGCTATGTCCCAACATGCTGGCATCATCCCTATGCCGGCATC
GACCTTGCACTACGGAGACGCTCAAGAATGCTGGCATCAGCAGTGCAGTGAACAGGCC
GGACCCCCGGCTTGTGCTCTGGCCTGTGGCACCATTGCTCAGTACCTGTGGCCAGCTGG
CCAGCTACCCCTGGGCTTAGTCAGGACCCGGATGCGAGGCCAACGCTCTATTGAGGGCGT
CCGGAGGTGACCATGAGCAGCCTTCAAAACATATCCTGCGGACCGAGGGGCCCTCGGGCT
GTACAGGGGGCTGGCCCCAACCTCATGAAGGTCACTCCAGCTGTGAGCATTCAAGCTACGTGG
TCTACGAGAACCTGAAGATCACCTGGCGTGCAGTCGGGTG**TGAC**GGGGGGAGGGCCGCC
GCAGTGGACTCGCTGATCCTGGCCGAGCCTGGGGTGTGCAGCCATCTCATTCTGTGAATG
TGCCAACACTAACGCTGTCTCGAGCCAAGCTGTGAAAACCTAGACGCACCCGCAAGGGAGGGT
GGGGAGAGCTGGCAGGCCAGGGCTTGTCTGCTGACCCAGCAGACCCCTCTGGTGGTCC
AGCGAAGACACAGGCACTCTCTAGGGTCCAGGGTCAAGCAGCAGCTCCGGGCTCACATGTGTA
GGACAGGACATTCTGAGTGGCTGCCAATAGTGAAGCTGGAGCCTGGAGGCCCCCTTAGT
TCTCCATTTCACCCCTGAGCAGCCAGCTGTGGCCACGGCCCTGCCCCTCTGGTCTGCCGTGC
ATCTCCCTGTGCCCTTGCTGCCCTGCTGAGGTAAAGGTGGAGGAGGGCTACAG
CCCACATCCCACCCCTCGTCAAATCCATAATCCATGATGAAAGGTGAGGTACGTGGCCT
CCCAGGCTGACTTCCAACCTACAGCATTGACGCCAATTGGCTGTGAAGGAAGAGGAAAG
GATCTGGCCTTGTGGTCACTGGCATCTGAGCCCTGCTGATGGCTGGGCTCTCGGGCATG
TGGGAGTGAGGGGCTGGGCTGCCCTGCCCTGGCTGCACAGAAGGCAAGTGTGGGGCTCA
TGGTCTCTGAGCTGGCCTGGACCCCTGTCAGGATGGGCCCCACCTCAGAACAAACTCAGT
TCCCCACTGTGGCATGAGGGCAGTGGAGCACCATGTTGAGGGCAGAGGGCAGAGCGTTGT
GTGTTCTGGGAGGGAGGGAAAAGGTGTTGGAGGCCCTAATTATGGACTGTGGGAAAAGGG
TTTGTCCAGAAGGACAAGCCGACAAATGAGCAGCTGTGCTTCCAGAGGAAGACGAGG
GAGCAGGAGCTGGCTGACTGCTCAGAGTCTGACGCCCTGGGGCTCTGTCCAACC
CCAGCAGGGGCGCAGCGGACAGCCCCACATTCAACTGTGTCAGTGTGGAAACCTATT
ATTTGTATTATTGAACAGAGTTATGCTTAACATTTTATAGATTGTTAATTAA
GCTGTCTTCAAGTCATTTCATATTATGTTATGGTGTACCTTCCC
AAGCCCGCCCACTGGGATGGGAGGGAGGAGAAGGGGGCCTGGGGCGCTGCACT
CTGTCAGAGAAATTCTTGGGACTGGAGGGAGAAGGGCTTGGCCCCAGCCTTAGGATTTCAGGGTTGA
CTGGGGCGTGGAGAGAGAGGGAGAACCTCAATAACCTGAAGGTGGAAATCCAGTTATT
CTGCGCTGCCAGGGTTCTTATTCACTCTTCTGAATGTCAAGGCAGTGAGGTGCCTCT
CACTGTGAATTGTGGTGGCGGGGGCTGGAGGAGGGTGGGGGCTGGCTCCGTCCCTCC
CAGCCTTGTGCCCTGCTTAACAATGCCGCCACTGGCAGCTCACGGTTGCACTTCC
ATTCCACCAAGAACGACTGATGAGGAATCTCAATAGGATGCAAAGATCAATGCAAAATT
GTTATATATGAACATATAACTGGAGTCGCAAAAAGCAAATTAGGAAAGAATTGGACGTTAG
AAGTTGTCAATTAAAGCAGCCTCTAATAAAAGTTGTTCAAAGCTGAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 206

MLCLCLYVPVIGEAQTEFQYFESKGLPAELKSIFKLSVFIPSQEFSTYRQWKQKIVQAGDKD
LDGQLDFEEFVHYLQDHEKKLRLVFKILDKKNDGRIDAQEIMQSLRDLGVKISEQQAEKILK
SMDKNGTMTIDWNEWRDYHLLHPVENIPEIILYWKSTIFDVGENLTVPDEFTVEERQTGMW
WRHLVAGGGAGAVSRTCTAPLDRLKVLMQVHASRSNNMGIVGGFTQMIREGGARSLWRNGI
NVLKIAPESAIKFMAYEQIKRLVGSQETLRIHERLVAGSLAGAIAQSSIYPMEVLKTRMAL
RKTGQYSGMLDCARRILAREGVAAFYKGYVPNMLGIIPYAGIDLAVYETLKNawlQHYAVNS
ADPGVFVLLACGTMSSCGQLASYPLALVRTRMQAQASIEGAPEVTMSSLFKHILRTEGAFG
LYRGLAPNFMKVIPAVSISYVVYENLKITLGVQSR

Important features:**Signal peptide:**

amino acids 1-16

Transmembrane domain:

amino acids 284-304, 339-360, 376-394

Mitochondrial energy transfer proteins signature.

amino acids 206-215, 300-309

N-glycosylation site.

amino acids 129-133, 169-173

Elongation Factor-hand calcium-binding protein.

amino acids 54-73, 85-104, 121-140

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FIGURE 207

GGAAGGCAGCGGCAGCTCCACTCAGCCAGTACCCAGATAACGCTGGAACCTCCCCAGCC**AT**
GGCTTCCCTGGGCAGATCCTCTTCTGGAGCATAATTAGCATCATCATTATTCTGGCTGGAG
CAATTGCACTCATCATTGGCTTGGTATTCAGGGAGACACTCCATCACAGTCACTACTGTC
GCCTCAGCTGGAACATTGGGAGGATGGAATCCTGAGCTGCACTTTGAACCTGACATCAA
ACTTTCTGATATCGTGTGATACAATGGCTGAAGGAAGGTGTTAGGCTTGGTCCATGAGTTCA
AAGAAGGCAAAGATGAGCTGTCGGAGCAGGGATGAAATGTTCAAGAGGCCGGACAGCAGTGT
GCTGATCAAGTGATAGTTGGCAATGCCTTTGCGGCTGAAAAACGTGCAACTCACAGATGC
TGGCACCTACAAATGTTATATCATCACTCTAAAGGCAAGGGGAATGCTAACCTTGAGTATA
AAACTGGAGCCCTCAGCATGCCGGAAAGTGAATGTGGACTATAATGCCAGCTCAGAGACCTTG
CGGTGTGAGGCTCCCGATGGTCCCCAGCCCACAGTGGCTGGCATCCAAAGTTGACCA
GGGAGCCAACCTCTCGGAAGTCTCAATACCAGCTTGAGCTGAACTCTGAGAATGTGACCA
TGAAGGTTGTGCTGTGCTACAATGTTACGATCAACAACACATACTCCTGTATGATTGAA
AATGACATTGCCAAAGCAACAGGGATATCAAAGTGACAGAATCGGAGATCAAAAGGCGGAG
TCACCTACAGCTGCTAAACTCAAAGGCTCTGTGTCTCTTCTTGCATCAGCT
GGGCACTTCTGCCCTCAGCCCTACCTGATGCTAAA**TAAT**GTGCCCTGGCCACAAAAAG
CATGCAAAGTCATTGTTACAACAGGGACTACAGAACTATTCACCACAGATATGACCTAG
TTTATATTCTGGGAGGAAATGAATTCATATCTAGAAGTCTGGAGTGAGCAAACAAGAGCA
AGAAAACAAAAAGGCCAAAGCAGAAGGCTCAATATGAACAAGATAATCTATCTCAA
GACATATTAGAAGTTGGGAAAATAATTGATGTGAACTAGACAAGTGTGTTAAGAGTGATAAG
TAAAATGCACGTGGAGACAAGTGCATCCCCAGATCTCAGGGACCTCCCCCTGCCGTACCT
GGGGAGTGAGAGGACAGGGATAGTCATGTTCTTGTCTGAAATTAGTTATATGTGCTG
TAATGTTGCTCTGAGGAAGCCCTGGAAAGTCTATCCAAACATATCCACATCTTATATTCCA
CAAATTAAGCTGTAGTATGTACCCCTAACAGACGCTGCTAATTGACTGCCACTCGCAACTCAGG
GGCGGCTGCATTTAGTAATGGGTCAAATGATTCACTTTATGATGCTTCAAAGGTGCCT
TGGCTTCTCTCCAACTGACAAATGCCAAAGTTGAGAAAATGATCATAATTAGCATAA
ACAGAGCAGTCGGGGACACCGATTAAATAACTGAGCACCTTCTTTAAACAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 208

MASLGQILFWSIISIIILAGAIALIIGFGISGRHSITVTTVASAGNIGEDGILSCTFEPDI
KLSDIVIQWLKEGVGLVHEFKEGKDELSEQDEMFRGRTAVFADQVIVGNASLRLKNVQLTD
AGTYKCYIITSKGKGNANLEYKTGAFSMPEVNVDYNASSETLRCEAPRWFPQPTVVWASQVD
QGANFSEVSNTSFELNSENVTMKVSVLYNVTINNTYSCMIENDIAKATGDIKVTESEIKRR
SHLQLLNSKASLCVSSFFAISWALLPLSPYLMNK

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FIGURE 209

GAATTGTAGAAGACAGCGCGTTGCCATGGCGCGTCTCTGGGCAGGTGTTGGCTCTGGT
GCTGGTGGCCGCTCTGTGGGTGGCACGCAGCCGCTGCTGAAGCGGGCTCCGCCGGCCTGC
AGCGGGTTCATGAGCCGACCTGGGCCAGCAGTGCTACAGGAGATGAAGACCCCTTCTTG
AATACTGAGTACCTGATGCCCTTCTCCTCAACCAGTGTGGATCCCTCTATTACCTCAC
CTTGGCATCGACAGATCTGACCCCTGGCTGTGCCATCTGTAACTCTCTGGCTATCATCTCA
CACTGATTGGTGGGAAGGCCCTGGAGAAGATATTGGTGGAAAACGTAAGTTAGACTACTGC
GAGTGCAGGGACGCAGCTGTGGATCTGACACACCTGTGTTAGTCCTCCCAGAACCCAT
CTCCCCAGAGTGGGTGAGGACACGCCCTTCCCACCTGCCCTTCCTGAGCTGTT
GCTTCCTTGCCATCAGAGTCCCTCCCTGGACAGTCTGGAGAAAGACAGAGGCTGGG
GTTTGGGATTGAAGACCAGACCCATCTGAGCCCTCCAGCCCTGTACAGCTCCTACT
GGCATGGCTGAGCTCAGACCCCTCTGATTCTGCCTATTATCCCAGGAGCAGTTGCTGGCAT
GGTGCCTACCGTGATAGGAATTCACTCTGCATCACAAGCTCAGTGAGTAAGACCCAGGGGC
AACAGTCTACCCCTTGAGTGGCGAACCCACTCCAGCTCTGCTGCCCTCAGGAAGCCCT
GGCCATGAAGTGTGGCAGTGAGCGGATGGACCTAGCACTCCCTCTGGCCTAGCTT
CCTCCCTCTTATGGGATAACAGCTACCTCATGGATCACAATAAGAGAACAGAGTGAAG
AGTTTGTAACCTCAAGTGCTGTTCACTGCTGCCCCAGCAGCTCTTCCCTGCTAACATCT
CCCTCAGCAACCTTCTGCCCTGATCTGGACTATCATGGTGGCAGGTTCCATGGACTGCAGAACT
GCCACCATTACTGTGGCCTGATCTGGACTATCATGGTGGCAGGTTCCATGGACTGCAGAACT
CCAGCTGCATGGAAAGGCCAGCTGCAGACTTGAGCCAGAAATGCAAACGGGAGGCCTCTG
GGACTCAGTCAGAGCGCTTGGCTGAATGAGGGGTGGAACCGAGGGAAAGAGTGCCTGG
GTGGCAGATGCAGGAAATGAGCTGTCTATTAGCCTGCCCTGCCCAACCATGAGGTAGGCAG
AAATCCTCACTGCCAGCCCTCTAACAGGTAGAGAGCTGTGAGCCCCAGCCCCACCTGAC
TCCAGCACACCTGGCGAGTAGTAGCTGTCAATAATCTATGTAAACAGACAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 210

MAASLGQVLALVLVAALWGQTQPLLKRASAGLQRVHEPTWAQQLQEMKTLFLNTEYLMMPFL
LNQCGSLLYYLTLASTDLTLAVPICNSLAIIFTLIVGKALGEDIGGKRKLDYCECGTQLCGS
RHTCVSSFPEPISPEWVRTRPFPILPFPLQLFCFLVAIRVPPWTVWRKTEAGVWD

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FIGURE 211

CTTCTGTAGGACAGTCACCAGGCCAGATCCAGAAGCCTCTCTAGGCTCCAGCTTCTGTG
GAAGATGACAGCAATTATAGCAGGACCCGCCAGGCTGTCGAAAAGATTCCGCAATAAAACT
TTGCCAGTGGGAAGTACCTAGTGAAACGCCCTAAGATGCCACTTCTCATGTCCCAGGCT
TGAGGCCCTGTGGTCCCCATCCTTGGGAGAAGTCAGCTCCAGCACCTGAAGGGCATTCTCG
TTGCTGGTATCACTGCAGTGCTTGCAGCTGTAGAATCTCTGAGCTGCGTGCAGTGTAAAT
TCATGGAAAAATCCTGTGTCAACAGCATTGCCCTCTGAATGTCCTCACATGCCAACACAG
CTGTATCAGCTCCTCAGCCAGCTCCTCTAGAGACACCAGTCAGATTATACCAGAATATGT
TCTGCTCAGCGGAGAACTGCAGTGAGGAGACACACATTACAGCCTTCACTGTCCACGTGTCT
GCTGAAGAACACTTCATTTGTAAGCCAGTGCTGCCAAGGAAAGGAATGCAGCAACACAG
CGATGCCCTGGACCCTCCCTGAAGAACGTGTCCAGCAACGCCAGAGTGCCCTGCTTGTATG
AATCTAATGGAACCTCCTGTGTGGGAAGCCCTGGAAATGCTATGAAGAAGAACAGTGTGTC
TTCTAGTTGCAGAACTTAAGAATGACATTGAGTCTAAGAGTCTCGTGTGAAAGGCTGTT
CAACGTCAGTAACGCCACCTGTCAGTTCCGTCTGGTGAACAGACTCTGGAGGAGTCA
TCTTCGAAAGTTGAGTGTGCAAATGTAACAGCTTAACCCCCACGTCTGCACCAACCACT
TCCCACAAACGTGGCTCCAAAGCTCCCTTACCTCTTGGCCCTTGCCAGCCTCCTCTCG
GGGACTGCTGCCCTTGAGGTCTGGGCTGCACTTGCCAGCACCCATTCTGCTTCTG
AGGTCCAGAGCACCCCCCTGCGGTGCTGACACCCTTTCCCTGCTCTGCCCCGTTAACTGC
CCAGTAAGTGGGAGTCACAGGTCTCCAGGCAATGCCGACAGCTGCCCTGTTCTCATTATTA
AAGCACTGGTTCACTGCCAaaaaaaaaaaaaaaaaaaaaaaa

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FIGURE 212

MKGILVAGITAVLVAAVESLSCVQCNWEKSCVNSIASECPHANTSCISSSASSSLETPVR
LYQNMFCSAENCSEETHITAFTVHVSAAEEHFHFVSQLCQGKECSNTSDALDPLKNVSSNAE
CPACYESNGTSCRGKPWKCYEEEQCVFLVAELKNDIESKSLVLKGCSNVSNATCQFLSGENK
TLGGVIFRKFECANVNSLPTSAPTTSHNVGSKASLYLLALASLLLRGLLP

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FIGURE 213

GGCCTCGTTCAAACGACCCGGTGGGTCTACAGCGGAAGGGAGGGAGCGAAGGTAGGAGGCA
GGGCTTGCCTCACTGGCCACCCCTCCAACCCCAAGAGGCCAGCCCC **ATGGT**CCCCGCCGCC
GCGCGCTGCTGTGGTCCTGCTGCTGAATCTGGTCCCCGGCGGGGGCCCAAGGCCTG
ACCCAGACTCCGACCGAAATGCAGCGGGTCAGTTACGCTTGGGGGCCATGACCCGCAG
CTACCGGAGCACGCCGGACTGGCTTCCCCGGAAGACAAGGATAATCCTAGAGGACGAGA
ATGATGCCATGGCGACGCCGACCGCCTGGCTGGACAGCGGCTGCCAGCTTGGCGCC
ACGGTGTCCACCGGTTAGCCGGTGTCCGCCATTAACGAGGAGGATGGGTCTCAGAAGA
GGGGTTGTGATTAATGCCGAAAGGATAGCACCGAGAGAGCTTCCAGTGCAGCTCCCA
ATACAGCGGGAGTTCCAGCACGAGGTTATAGCCAATAGTCAGGAGCCTGAAATCAGGCTG
ACTTCAAGCCTGCCCGCTCCCCGGAGGTCTACTGAGGACCTGCCAGGCTCGCAGGCCAC
CCTGAGCCAGTGGTCCACACCTGGGTCTACCCCGAGCCGGTGGCCGTACCCCTACCCACAG
CCATGCCATCTCCTGAGGATCTCGGGCTGGTGCTGATGCCCTGGGGCCGTGGCACTGCCAC
TGCAAGTCGGCACCATGAGCCGGAGCCGGTCTGGGAAGCTGCACGCCCTTCCGGCGCCT
TCGAGTTGGGCGCTGAGCCAGCTCCGCACGGAGCACAGCCTTGACACCTATCAACAATGTC
CCTGCAACCGACTTCGGGAAGAGTGCCCCCTGGACACAAGTCTCTGTACTGACACCAACTGT
GCCCTCTCAGAGCACCACCACTACCAAGGACCCACTACCCCTCCCCACCATCCACCTCAG
AAGCAGTCCCAGCCTGCCACCCGCCAGCCCCTGCCAGCCCTGGTTGGAAACGGGTCA
GGATTGGCCTGGAGGATATTGGAATAGCCTCTTCAGTGTTCACAGAGATGCAACCAATA
GACAGAAACCAAGAGG **TAAT**GGCCACTTCATCCACATGAGGAGATGTCAGTATCTAACCTCT
CTTGCCCTTCAATCCTAGCACCCACTAGATATTTAGTACAGAAAAACAAAATGGAAAA
CACAA

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FIGURE 214

MVPAAGALLWVLLNLGPRAAGAQGLTQTPTEMQRVSLRFGGPMTRSYRSTARTGLPRKTRI
ILEDENDAMADADRLAGPAAAELLAATVSTGFSRSSAINEEDGSSEEGVVINAGKDSTSREL
PSATPNTAGSSSTRFIANSQEPEIRLTSSLPRSPGRSTEDLPGSQATLSQWSTPGSTPSRWP
SPSPPTAMPSPEDLRLVLMPWGPWHCHCKSGTMSRSRSGKLHGLSGRLRVGALSQLRTEHKPC
TYQQCPCNRLREECPLDTSLCDTNCASQSTTSTRTTTPFPTIHLRSSPSLPPASPCPALA
FWKRVRIGLEDIWNSLSSVFTEMQPIDRNQR

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FIGURE 215

CCCGGGTCACCCACGGTCCGGGGAGAAAGGATGCCGGCTGGCGCGGGTGGCCTGCTAGCTGGGCA
GCCGGCCTGGCGAGCGCTCCAGGGCACCCTGAGCGGTGACCGCAGCTGGTACTGCAGTGCAGAGACA
GAACCTGCTCTGGGGCGCTCTGAATCACTTCCGCTCCGCCAGCAATCTACATGAGTCTAGCAGGCTGGACCT
GTCGGGACGACTGTAAGTATGAGTGTATGTTGGCTACCGTTGGCTTACCTCCAGGAAGGTACAAAGTGCCT
CAGTTCCATGGCAAGTGGCCCTCTCCGGTCTCTGTTCTTCAGAGGCCGATCGGCCAGCCTCCCTCCCCATGTACCA
CAATGGCCTGGCAGCCTGGTGTGCTCTGCCGCTACCGCACCTCGTGCAGCCTCCCTCCCCATGTACCA
CCTGTGTGGCCTCGCCTGGTGTCCCTCAATGATGGTCTGGTCCACAGTCTTCCACACCAGGGACACTGAC
CTCACAGAGAAAATGGACTACTTCTGTGCTCCACTGTATCCTACACTCAATCTACCTGTGCTGCGTCAGGAC
CGTGGGCTGCAGCACCCAGCTGTTGAGTGCCTCCGGCTCTCTGCTGCTCATGCTGACCGTGCACGTCT
CCTACCTGAGCCTCATCCGCTTCGACTATGGCTACAACCTGGTGGCAACGTGGTATTGGCCTGGTCAACGTG
GTGTTGGCTGGCTGGCTGTGAGACCAGCGGCGCTGCCTCACGTGCGCAAGTGCAGGGTGGTGGTCTT
GCTGCTGCAGGGGCTGTCCTGTCAGGCTGCTGACTTCCACCGCTCTTCTGGTCTGGATGCCATGCCA
TCTGGCACATCAGCACCATCCCTGTCACGCTCTTCACTGGAGATGACAGCCTGTACCTGCTG
AAGGAATCAGAGGACAAGTCAAGCTGGACTGAAGACCTTGAGCGAGTGCCTGGGAGTGGGATCCTGCC
GCCCTGCTGGCCTCCCTCCCTCAACCCCTTGAGATGATTCTCTTCAACTTCTGAACCTGGACATGA
AGGATGTGGCCCAGAATCATGTGGCAGCCCACCCCTGTTGGCCTCACAGCCTGGAGTCTGTTCTAGG
AAGGCCTCCCAGCATCTGGACTCGAGAGTGGCAGCCCCTCACCTCTGGAGCTGAACCTGGGTTGA
GTGTTCTTAGCTCTACCCGGAGGACAGCTGCTGTTCTCCCTCCACAGCCTCTCCACATCCCCAGCTG
CCTGGCTGGGCTCTGAAGCCCTGTCTACCTGGAGACCAGGGACCACAGCCTTAGGGATA
CAGGGGTTCC
CTTCTGTTACCAACCCCAACCCCTCCAGGACACCAACTAGGTGGTGTGGATGCTTGTCTTGGCAGCAA
GGTTCACGGCAGATTCTCCCATGGATCTTGAGGGACCAAGCTGCTGGGATTGGGAAGGAGTTCA
CTGGCCCTAGCCAGGTTCCCAGGAGGCTCACCATACTCCCTTCAGGGCAGGGCTCCAGCAAGCCCAGGGCA
AGGATCTGTGCTGCTGTTGAGAGCCTGCCACCGTGTGCGGGAGTGTGGCAGGCTGAGTGCATAGG
TGACAGGGCCGTGAGCATGGCCTGGTGTGAGCTCAGGCTTAGGTGCGCAGTGTGGAGACGGGTGTTG
CGGGGAAGAGGTTGGCTCAAAGTGTGTTGAGGAGCTGACTGCTGGAGGAGTGTGGAGCAGGAT
TGCGCGTGTGGTGGCATGTGAGATGAGTGTGACTGCTGGAGGAGTGTGGAGCAGGAT
GAGGGAACTCTGTACCATCAATAATCCTGGAGGAGGAGTGTGGAGGAGTGTGGAGCAGG
CAGGAGCTCTCATGGCCAGGCTGCCATGTGCTGAGTGTGGTGTGCTGGTGCCTGCTGGTGC
CTCACAGGGTCCCCACACAAGTGCCTCCAGAAGCAGCCCCTGGAGGCAGAGGAAGGAAAATGGGATGGC
TGGGCTCTCCATCCTCTTCTGCTGCCATGGCTGGCCTCCCTCCAAACCTCCATTCC
GCTGCCAGCCCCCTTGCCATAGCCTGATTGGGGAGGAGGAAGGGGCAATTGAGGGAGAAGGGGAGAAGCT
TATGGCTGGCTGTGGTTCTCCCTCCAGAGGGCTTACTGTTCCAGGGTGGCCCCAGGGCAGGCAGGGGCC
ACACTATGCCGTGCCCTGGTAAAGGTGACCCCTGCCATTACAGCAGCCCTGGCATGTTCTGCC
AAATAGAATGGAGGGAGCTCCAGAAACTTCCATCCAAAGGCAGTCTCCGTGGTGAAGCAGACTGGATT
CTCTGCCCTGACCCCTTGTCCCTCTTGAGGGAGGGAGCTATGCTAGGACTCCAACCTCAGGGACTGGGTG
GCCTGCCAGCTAGCTTGTGACTGAAACTTTAAGGTGGAGGGTGGCAAGGGATGTGCTTA
TTCCAAGCCTCAAAAAAAAAAAAAAA

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FIGURE 216

MAGLAARLVLLAGAAALASGSQGDREPVYRDCVLQCEEQNCSGGALNHFRSRQPIYMSLAGW
TCRDDCKYECMWTVGLYHQEGHKVPQFHGKWPFSRFLFFQEPASAVASFLNGLASLVMLCR
YRTFVPASSPMYHTCVAFAWVSLNAWFWSTVFHTRDTDLTEKMDYFCASTVILHSIYLCCVR
TVGLQHPAVVSAFRALLMLTVHVSYLSLIRFDYGYNLVANVAIGLVNVVWWLAWCLWNQR
RLPHVRKCVVVVLLQGLSLLDFPPLFWVLDAHAIWHISTIPVHVLFFSFLEDDSLYLL
KESEDKFKLD

Important features:**Signal peptide:**

amino acids 1-20

Transmembrane domains:

amino acids 105-123, 138-156, 169-185, 193-209, 221-240, 256-272

N-glycosylation site.

amino acids 40-44

N-myristoylation site.

amino acids 43-49

CUB domain proteins profile.

amino acids 285-302

Amiloride-sensitive sodium channels proteins.

amino acids 162-186

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FIGURE 217

GGCCGCCTGGAATTGTGGGAGTTGTCTGCCACTCGGCTGCCGGAGGCCGAAGGTCCGTGA
CTATGGCTCCCCAGAGCCTGCCTTCATCTAGGATGGCTCCTCTGGCATGCTGCTTGGCTG
CTGATGGCCGCCTGCTTCACCTCTGCCTCAGTCATCAGAACCTGAAGGAGTTGCCCTGAC
CAACCCAGAGAAGAGCAGCACCAAAGAAACGGAGAGAAAAGAAACCAAAGCCGAGGAGGAGC
TGGATGCCGAAGTCCTGGAGGTGTTCCACCCGACGCATGAGTGGCAGGCCCTCAGCCAGGG
CAGGCTGTCCCTGCAGGATCCCACGTACGGCTGAATCTCAGACTGGGAAAGAGAGGCAAA
ACTCCAATATGAGGACAAGTCCGAAATAATTGAAAGGAAAAGGCTGGATATCAACACCA
ACACCTACACATCTCAGGATCTCAAGAGTGCAGTGGCAAAATTCAAGGAGGGGGCAGAGATG
GAGAGTTCAAAGGAAGACAAGGCAAGGCAGGCTGAGGTAAAGCGGCTCTCCGCCATTGA
GGAAGTGAAGAAAGACTTGATGAGCTGAATGTTGTCATTGAGACTGACATGCAGATCATGG
TACGGCTGATCAACAAGTTCAATAGTTCCAGCTCCAGTTGGAAGAGAAAGATTGCTGCGCTC
TTTGATCTTGAATATTATGTCCATCAGATGGACAATGCGCAGGACCTGCTTCCCTTGGTGG
TCTTCAAGTGGTGATCAATGGCTGAACAGCACAGAGCCCTCGTAAGGAGTATGCTGCGT
TTGTGCTGGCGCTGCCCTTCAGCAACCCCAAGGTCCAGGTGGAGGCCATGAAGGGGA
GCCCTGCAGAAGCTGCTGGTCATCCTGCCACGGAGCAGCCGCTACTGCAAAGAAGAAGGT
CCTGTTGCACTGTGCTCCCTGCTGCCACTTCCCTATGCCAGGGCAGTCCCTGAAGC
TCGGGGGGCTGCAGGTCTGAGGACCTGGTCAGGAGAAGGGCACGGAGGTGCTCGCGTG
CGCGTGGTCACACTGCTTACGACCTGGTCACGGAGAAGATGTTGCCAGGGAGGAGGCTGA
GCTGACCCAGGAGATGTCCCCAGAGAAGCTGCAGCAGTATGCCAGGTACACCTCCGCCAG
GCCCTGTGGGAACAGGGCTGGTGCAGGATCACGCCACCTCCCTGGCGCTGCCGAGCATGAT
GCCCGTGAGAAGGTGCTGCAGACACTGGCGTCCCTGACCACCTGCCGGACCGCTACCG
TCAGGACCCCCAGCTGGCAGGACACTGCCAGCAGGCTGAGTACCAAGGTGCTGGCCA
GCCCTGGAGCTGCAGGATGGTGAGGACGAGGGCTACTCCAGGAGTGTGGCTCTGTCAAC
AGCTTGCTGAAGGAGCTGAGATGAGGCCACACCAGGACTGGACTGGATGCCCTAGTGA
GGCTGAGGGGTGCCAGCGTGGTGGCTCTCAGGCAGGAGGACATCTGGCAGTGCTGGCT
TGGCCATTAAATGAAACCTGAAGGCCAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 218

MAPQSLPSSRMAPLGMILLGILMAACFTFCLSHQNLKEFALTNPEKSSTKETERKETKAEEEL
DAEVLEVFPTHEWQALQPGQAVPAGSHVRLNLQTGEREAKLQYEDKFRNNLKGKRLDINTN
TYTSQDLKSALAKFKEGAEMESSKEDKARQAEVKRLFRPIEELKKDFDELNVVIETDMQIMV
RLINKFNSSSSLEEKIAALFDLEYYVHQMDNAQDLLSFGGLQVINGLNSTEPLVKEYAAF
VLGAAAFSSNPKVQVEAIEGGALQKLLVILATEQPLTAKKVLFALCSLLRHFPYAQRQFLKL
GGLQVLRTLVQEKGTEVLAVRVVTLLYDLVTEKMFAEEEAEELTQEMSPEKLQQQYRQVHLLPG
LWEQGWCEITAHLLALPEHDAREKVLQTLGVLLTCDRYRQDPQLGRTLASLQAEYQVLAS
LELQDGEDEGYFQELLGSVNSLLKELR

Important features:

Signal peptide:

amino acids 1-29

Hypothetical YJL126w/YLR351c/yhcX family protein.

amino acids 364-373

N-glycosylation site.

amino acids 193-197, 236-240

N-myristoylation site.

amino acids 15-21, 19-25, 234-240, 251-257, 402-408, 451-457

Homologous region SLS1 protein.

amino acids 68-340

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FIGURE 219

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FIGURE 220

MGAAVFFGCTFVAFGPALFLITVAGDPLRVIILVAGAFFWLVSLLASVVFILVHVTDR
SDARLQYGLLIFGAAVSVLLQEVFRFAYYKLLKADEGLASLSEDGRSPISIRQMAYVSGLS
FGIIISGVFSVINILADALGPGVVGIGHGDSPYYFLTSAAIIILLHTFWGVVFFDACCRR
YWALGLVVGSHLLTSGLTFLNPWYEASLLPIYAVTVSMGLWAFITAGGSLRSIQRSLCKD

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FIGURE 221

AAGCTGGTTAAGGAAGCAGAGGAGGGTAGATTGTTGAGTGAGGACGGAAGATCAACCCA
TTTCCATTCCGCCAGATGGCCTATGTTCTGGTCTCTCCCTCGGNATCATCAGTGGTNT
TNTCTGTTATCAATATTTGGCTGATGCANTGGGCCAGGTGTGGTTGGGATCCATGGAGAC
TCACCCATTANTTCCTGANTTCAGCCTTNTGACAGCAGCCATTATCCTGCTC

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FIGURE 222

GACCGACC GTTCAGATGCCCGGTTCCAGTACGGCTCCTGATTTGGTGCTGCTGTNTCTG
TCCTTCTACAGGAGGTGTTCCGCTTGCCTANTACAAGCTGCTTAAGAAGGCAGATGAGGGG
TTAGCATNGCTGAGTGAGGACGGAAGATCACCCATTCCATCCGCCAGATGGCCTATGTTN
TGGTNTTCCTCGGTATCATCAGTGGTGTNTCTGTTATCAATATTTGGNTGATGCAN
TTGGGCCAGGTGTGGTTGGATCCATGGAGANTCACCTATTAATTCCCTGAATT CAGCCTT
NTGACAGCAGCCATTATCCTGNCCATACCTTTGGGGAGTTGTGTTTGATGCCTGTGA
GAGGAG

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FIGURE 223

NGTTGGAGAAGTGGCGCGGACNTTCATTGGGGTTCGGTTCCCCCTTCCCTTCCCCG
GGGTCTGGGGTGACATTGCACGGGCCCTCGTGGGTGCGTTGCCACCCCACGCGGACTCC
CCAGNTGGNGCGCCCTTCCCATTGCCTGTCCTGGTCAGGCCCAACCCCCCTTCCCACNTG
ACCAGCCATGGGGCTGCGGTGTTTCCGGCTGCACTTCGTCGCGTTGGCCGGCGCTTCG
CGCTTTCTGATCACTGTGGCTGGGACCCGCTTCGCGTTATCATCCTGGTCGCAGGGCA
TTTTCTGGCTGGTCTCCCTGCTCCTGGCCTCTGTGGTCTGGTCATCTGGTCCATGTGAC
CGACCGGTCAAGATGCCCGCTCCAGTACGGCCTCTGATTTGGTGCTGCTGTCTGTCC
TTCTACAGGAGGTGTTCCGCTTGCCACTACAAGCTGCTTAAGAAGGCAGATGAGGGTTA
GCATCGCTGAGTGAGGACGGAAGATCACCATCTCCATCCGCCAGATGGCCTATGTTCTGG
TCTCTCCTTCGGTATCATCAGTGGTGTCTCTGTTATCAATATTTGGCTGATGCACTTG
GGCCAGGTGTGGTTGGGATCCATGGAGACTCACCC

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FIGURE 224

GTAAAAGAAAGTGGCCGGACCTCATTGGGGTTCGGTTCCCCCTTCCCNTCCCCGGGG
TCTGGGGGTGACATTGCACCGCGCCNTCGTGGGTCGCCTGCCACCCACGCCGGACTCCC
CAGNTGGCGCGCCCTCCCATTGCCTGTCCTGGTCAGGCCCCCACCCCCCTTCCCACCTGA
CCAGCCATGGGGCTGCGGTGTTTCGGGCTGCACTTCGTCGCCCTCGGTCAGGGCCTTC
GCGCTTTCTTGATCACTGTGGCTGGGACCCGCTCGCTATCATCCTGGTCGCAGGGC
ATTTTCTGGCTGGTCTCCCTGCTCCTGCCCTGTGGTCTGGTCATCTGGTCCATGTGA
CCGACCGGTCAAGATGCCCGGCTCCAGTACGCCCTCGATTGGTCTGCTGTCTGTC
CTTCTACAGGAGGTGTTCCGCTTGCTACTACAAGCTGCTTAAGAAGGCAGATGAGGGTT
AGCATCGCTGAGTGAGGACGGAAGATCACCCATCTCCATCGCCAGATGGCCTATGTTCTG
GTCTCTCCTCGGTATCATCAGTGGTGTCTCTGTTATCAATATTTGGCTGATGCACCT
GGGCCAGGTGTGGTTGGGATCCATGGAGAC

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FIGURE 225

CCCCCAGGGAGCAGTGGGTGGTTATAACTCAGGCCCGGTGCCAGAGCCCAGGAGGAGGCAG
TGGCCAGGAAGGCACAGGCCTGAGAAGTCTGCGGCTGAGCTGGGAGCAAATCCCCCACCCCC
TACCTGGGGGACAGGGCAAGTGAGACCTGGTGAGGGTGGCTCAGCAGGCAGGGAAAGGAGAGG
TGTCTGTGCGTCCTGCACCCACATCTTCTCTGTCCCCTCCTGCCCTGTCTGGAGGCTGCT
AGACTCCTATCTTCTGAATTCTATAGTGCCTGGGTCTCAGCCAGTGCCATGGTGGCCCGT
CCTTGTGGTTCCTCTACCTGGGAAATAAGGTGCAGCGGCC**ATGG**CTACAGCAAGACCCC
CCTGGATGTGGGTGCTCTGTGCTGTGATCACAGCCTTGCTTCTGGGGTCACAGAGCATGTT
CTCGCCAACAATGATGTTCCCTGTGACCACCCCTCTAACACCGTGCCCTCTGGGAGCAACCA
GGACCTGGGAGCTGGGCCGGGAAGACGCCCGGTGGATGACAGCAGCAGCCGCATCATCA
ATGGATCCGACTGCGATATGCACACCCAGCCGTGGCAGGCCGCCTGTTGCTAAGGCCAAC
CAGCTCTACTGCGGGCGGTGTTGGTCATCCACAGTGGCTGCTCACGGCCGCCACTGCAG
GAAGAAAGTTTCAGAGTCCGTCTCGGCCACTACTCCCTGTCAACCAGTTATGAATCTGGC
AGCAGATGTTCCAGGGGTCAAATCCATCCCCACCCCTGGCTACTCCCACCCGGCCACTCT
AACGACCTCATGCTCATCAAACGTAAACAGAAGAATTGTCCTAAAGATGTCAGACCCAT
CAACGTCTCCTCTCATTGTCCTGCTGGACAAAGTGTGCTGGGTCTGGCTGGGGACAA
CCAAGAGCCCCAAGTCACCTCCCTAAGGTCCAGTGCTTGAATATCAGCGTGCTAAGT
CAGAAAAGGTGCGAGGATGCTTACCCGAGACAGATAGATGACACCATGTTCTGCGCCGGTGA
CAAAGCAGGTAGAGACTCCTGCCAGGGTGATTCTGGGGGCTGTGGTCTGCAATGGCTCCC
TGCAGGGACTCGTGTCCCTGGGAGATTACCTTGTGCCCGGCCAACAGACCGGGTGTCTAC
ACGAACCTCTGCAAGTTCACCAAGTGGATCCAGGAAACCATCCAGGCCAACTCC**TGAGTCAT**
CCCAGGACTCAGCACACCGGCATCCCCACCTGCTGCAGGGACAGCCCTGACACTCCTTCAG
ACCCCTATTCTTCCCAGAGATGTTGAGAATGTTCATCTCTCCAGCCCTGACCCATGTCT
CCTGGACTCAGGGTCTGCTCCCCACATTGGCTGACCGTGTCTCTAGTTGAACCCCTGG
GAACAATTCCAAAAGTCCAGGGCGGGGTTGCGTCTCAATCTCCCTGGGCACTTCAT
CCTCAAGCTCAGGGCCCACCCCTCTGCAGCTTGACCCAAATTAGTCCCAGAAATAAA
CTGAGAAGTGGAAAAAA

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FIGURE 226

MATARPPWMWVLCALITALLGVTEHVLANNVDSCDHPNSNTVPSGSNQDLGAGAGEDARSDD
SSSRIINGSDCDMHTQPWQAALLLRPNQLYCGAVILVHPQWLTAACRKVFRVRLGHYSLS
PVYESGQQMFQGVKSIPHGYSHPGHSNDLMLIKLNRRIRPTKDVRPINVSSHCPAGTKCL
VSGWGTTKSPQVHFVFKVLQCLNISVLSQKRCEDAYPRQIDDTMFCAGDKAGRSCQGDSGGP
VVCNGSLQGLVSWGDYPCARPNRPGVYTNLCKFTKWIQETIQANS

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FIGURE 227

ATGGTCAACGACCGGTGGAAGACCATGGCGCGCTGCCAACTTGAGGACCGGCCGCGCGA
CAAGCCGAGCGGGCGAGCTGCGGCTACGTGCTGCAACCGTGCTGCTGGCCCTGGCTGTG
TGCTGGCTGTAGCTGTCACCGGTGCCGTGCTTCTGAACCAACGCCACGCCGGGCACG
GCGCCCCCACCTGCGTCAGCACTGGGCTGCCAGGCCAACAGGCCCTGGTCACTGTGGA
AAGGGCGGACAGCTCGCACCTCAGCATCTCATTGACCCGCCGCTGCCCGACCTCACCGACA
GCTTCGCACGCCCTGGAGAGGCCAGGGCTCGGTGCTGCAGGCCGCTGACAGAGCACCAGGCC
CAGCCACGCCCTGGTGGCGACCAGGAGCAGGAGCTGCTGGACACGCCGACAGCTGCC
CCGGCTGCTGGCCCGAGCCTCAGAGCTGAGACGGAGTGCATGGGCTGCCGAAGGGCATG
GCACGCTGGGCCAGGGCCTCAGGCCCTGCAAGAGTGAAGCAGGCCGCTCATCCAGCTTC
TCTGAGAGCAGGGCACATGGCTCACCTGGTGAACTCCGTCAAGCACATCCTGGATGCCCT
GCAGAGGGGCCGGGGCTGGCCGGCCGCCAACAAAGGCCACCTTCAGAGAGGCCCTGCC
GGGGAAACCCGGCCGGGGCTGTGCCACTGGCTCCCGGCCAGACTGCTGGACGTCC
CTAAGCGGACAGCAGGACGATGGCTACTCTGTCTTCCACCCACTACCCGGCCGGCTT
CCAGGTGTACTGTGACATGCGCACGGACGGCGGCCGCTGGACGGTGTTCAGGCCGGAGG
ACGGCTCCGTGAACTCTTCCGGGCTGGGACGGTACCGAGACGGCTTGGCAGGCTCACC
GGGGAGCACTGGCTAGGGCTCAAGAGGATCCACGCCCTGACCACACAGGCTGCCACAGAGCT
GCACGTGGACCTGGAGGACTTTGAGAATGGCACGCCCTATGCCGCTACGGGAGCTTCGGCG
TGGGCTTGTCTCCGTGGACCCCTGAGGAAGACGGGTACCCGCTACCGTGGCTGACTATTCC
GGCACTGCAGGCAGCTCCCTCTGAAGCACGCCGATGAGGTTACCCACCAAGGACCGTGA
CAGCGACCATTCAGAGAACAACTGTGCCCTCTACCGGCTGGCTGGTGGTACCGCAACT
GCCACACGTCACCTCAATGGCAGTACCTGCGCGGTGCGCACGCCCTATGCCGACGGC
GTGGAGTGGTCCTCTGGACCGGCTGGCAAGTACTCACTCAAGTTCTGTAGATGAAGATCCG
GCCGGTCCGGGAGGACCGCTAGACTGGTGCACCTGTCTGGCCCTGCTGGTCCCTGTC
CCCATCCCCGACCCACCTCACTCTTCGTGAATGTTCTCACCCACCTGTGCCCTGGCGAC
CCACTCTCCAGTAGGGAGGGGCCATCCCTGACACGAAGCTCCCTGGGCCGGTGAAGT
CACACATGCCCTCTCGCGTCCCACCCCTCCATTGGCAGCTCACTGATCTTGCCTC
TGCTGATGGGGCTGGCAAACACTTGACGACCCCAACTCTGCTGCCCTACTGTAACCTCCGG
TGCTGTTGGCGTCCCTGGCAGGATGGTGGAGTCTGCCCCAGGACCCCTGTGCCCTGCC
GGCAAATACCCGGCATATTGGGAGAGAGCAGGGGGAGCAGCACCCCTGGAGTCTC
CTAGCAGATCGTGGGAATGTCAGGTCTCTGAGGTCTGAGGCCAGTATCCTCCAG
CCCTCCAAATGCCAACCCCCACCCGTTCCCTGGTGCCAGAGAACCCACCTCTCCCCAA
GGGCCTCAGCTGGCTGTGGCTGGGCTGGGCCATCCTACCAAGGCCCTGAGGTCAAGGATGG
GAGCTGCTGCCCTTGGGACCCACGCTCCAAGGCTGAGACCAAGTCCCTGGAGGCCACCCAC
CCTGTGCCCGGCAGGCCCTGGGCTGCACTCCTTACCTGCTGTGCCACCTGCTCTG
TCTCAAATGAGGCCAACCCATCCCCACCCAGCCTCCGGCGTCTCCCTACCTGGGCCAGC
CGGGGCTGCCATCCATTCTCTGCTGCCCTGGAAAGGTGGGCTGGGCCCTGCAACCGTGGGCT
GGACTGCGTAATGGGAAGCTCTGGTTCTGGGCTGGGCCCTAGGCAAGGGCTGGGATGAG
GCTTGTACAACCCCCACCAATTCCAGGGACTCCAGGGTCTGAGGCCCTCCAGGAGG
GCCTTGGGGGTGATGACCCCTTCCCTGAGGTGGCTGTCTCATGAGGAGGCCAACCTTGC
ATTGACCGTGGCCACCTGGACCCAGGCCAGGCCGGCCGGAGTGGTCAAGGGACAGGGA
CCACCTCACCGGGCAAATGGGTGGGGACTGGGCCACAGACAGGCCACCTGGACA
CTTCTTGTGAATCTCCAAACACCCAGCAGCTGTCACTCCACTCCTGTGACACA
TGCAGAGGTGAGACCCGCAGGCCAGGACCCAGCAGGCCACAGGCCAGGGCTGGAGGCCGG
TCCCTCAGCTGTGTCAGCAGGCCCTGGACCCCGCTGCGTTACGTCAGGCCAGATGCAAGGG
CGGCTTCTCAAGGCCCTCTGATGGGGCTCCGAAAGGGCTGGAGTCAGCCTTGGGAGCT
GCCTAGCAGCCTCTCCCTGGCAGGAGGGAGGTGGCTTCCCAAAGGACACCCGATGGCA
GGTGCCTAGGGGTGTGGGTTCCGTTCCCTCCACTGAAGTTGTGTTAAA
AACAATAAAATTGACTTGGCACCACGGGGTTGGAGAGGCCGTGTGACCTGGCTCTC
TGTCCCAGTGCCACCAGGTATCCACATGCCAG

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FIGURE 228

MVNDRWKTMGAAQLEDPRDKPQRPSCGYVLCTVLLALAVLLAVAVTGAFLFLNHAHAPGT
APPPVVSTGAASANSALVTVERADSSHLSILIDPRCPDLTDSFARLESAQASVLQALTEHQA
QPRLVGDQEELLDTLADQLPRLLARASELQTECMGLRKGHGTLGQGLSALQSEQGRLIQLL
SESEQHMAHLVNSVSDILDALQRDRGLGRPRNKADLQRAPARGTRPRGCATGSRPRDCLDVL
LSGQQDDGVYSVFPTHYPAGFQVYCDMRTDGGGWTVFQRREDGSVNFFRGWDAYRDGFGRLT
GEHWLGLKRIHALTTQAAAYELHVDLEDFENGAYARYGSFGVGLFSVDPEEDGYPLTVADYS
GTAGDSLLKHSGMRFTTKDRDSDHSENNCAAFYRGAWWYRNCHTSNLNGQYLRGAHASYADG
VEWSSWTGWQYSLKFSEM KIRPVREDR

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FIGURE 229

GCAGTCAGAGACTTCCCTGCCCTCGCTGGAAAGAACATTAGGAATGCCTTTAGTCCT
TGCTTCCTGAACTAGCTCACAGTAGCCGGCGGCCAGGGCAATCCGACCACATTCACTCT
CACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGCTGGATGATG
ATGGGGACACCAACCATGAGCCTGCATTCTCAAGCCTCTGCCACAACCTGGCATCCAGAGCCC
CGGCGCACAGAGCACAGGGCTCCCTTTCAACGTGGCGACCAGTGGCCTGACCCCTGCTGAC
TTTGTGCTTGGTGTGCTGATAGGGCTGGCAGCCCTGGGCTTTGTTTCAAGTACTACC
AGCTCTCCAATACTGGTCAAGACACCATTCTCAAATGGAAGAAAGATTAGGAAATACGTCC
CAAGAGTTGCAATCTCTCAAGTCCAGAATATAAGCTTGAGGAAAGTCTGCAGCATGTGGC
TGAAAAAACTCTGTCGTGAGCTGTATAACAAAGCTGGAGCACACAGGTGCAGCCCTGTACAG
AACAAATGGAATGGCATGGAGACAATTGCTACCAGTTCTATAAGACAGCAAAAGTTGGAG
GACTGTAAATATTCTGCCCTTAGTGAAACTCTACCATGCTGAAGATAAAACAAACAAGAAGA
CCTGGAATTGCCCGTCTCAGAGCTACTCTGAGTTTCTACTCTTATTGGACAGGGCTT
TGCGCCCTGACAGTGGCAAGGCCCTGGCTGTGGATGGATGGAACCCCTTCACTCTGAAC
TTCCATATTATAATAGATGTCACCAGCCAAAGAACAGAGACTGTGTGGCCATCCTCAATGG
GATGATCTCTCAAAGGACTGCAAAGAATTGAAGCGTTGTGTGAGAGAACAGGAG
TGGTGAAGCCAGAGAGCCTCCATGTCCCCCTGAAACATTAGGCAAGGTGACTTCATGCC
CTCTGCAACTACAAATAGCAGAGTGAGCCAGGCGGTGCCAAGCAAGGGCTAGTTGAGACAT
TGGGAAATGGAACATAATCAGGAAAGACTATCTCTGACTAGTACAAATGGGTTCTCGTG
TTTCTGTTCAAGGATCACCAGCATTCTGAGCTGGTTATGCACGTATTAACAGTCACA
AGAAGTCTTATTTACATGCCACCAACCAACCTCAGAAACCCATAATGTCATCTGCCCTCTG
GCTTAGAGATAACTTTAGCTCTCTCAATGTCTAATATCACCTCCCTGTTCT
GTCTCCTTACACTGGTGGATAAGAAACTTTGAAGTAGAGGAAATACATTGAGGTAAC
ATCCTTTCTGACAGTCAGTAGTCCATCAGAAATTGGCAGTCACTCCAGATTGTACC
AGCAAATACACAAGGAATTCTTTGTTCTGAGTCATACTAGTCCCTCCAAATCCAT
CAGTAAAGACCCATCTGCCCTGTCCATGCCGTTCCAACAGGGATGTCACTGATATGAG
AATCTCAAATCTCAATGCCCTATAAGCATTCCCTGTGTCCTTAAGACTCTGATAATTG
TCTCCCTCCATAGGAATTCTCCAGGAAAGAAATATATCCCCATCTCGTTCATATCAG
AACTACCGTCCCCGATATTCCCTCAGAGAGATTAAGACCAAGAAAAAGTGAGGCTCTCA
TCTGCACCTGTAATAGTTCAAGTCCATTGACCCATATTACCTTCAG
GTACTGAAGATTAATAATAATGAAATACTGTGAAAAA

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FIGURE 230

MQAKYSSTRDMLDDGDTTMSLHSQASATTRHPEPRTTEHRAPSSTWRPVALTLTLCLVLL
IGLAALGLLFFQYYQLSNTGQDTISQMEERLGNTSQELQSLQVQNIKLAGSLQHVAEKLCRE
LYNKAGAHRCSPCTEQWKWHGDNCYQFYKDSKSWEDCKYFCLSENSTMLKINKQEDLEFAAS
QSYSEFFYSYWTGLLRPDSGKAWLWMDGTPFTSELFHIIIDVTSPRS RDCVAILNGMIFSKD
CKELKRCVCERRAGMVKPESLHVPPETLGEGD

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FIGURE 231

AATTTCACCGCTGTAGGAATCCAGATGCAGGCCAAGTACAGCAGCACGAGGGACATGNTGG
ATGATGATGGGACACCAACCATGAGCCTGCATTNTCAAGCTTTGCCACAATTGGCATCCAG
AGCCCCGGCGCACAGAGCACAGGGNTCCTTTCAACGTGGCGACCAGTGGCCCTGACCCTG
CTGACTTTGTGCTTGGTCTGCTGATAGGGCTGGCAGCCCTGGGCTTTGTTTTCAAGTA
CTACCAAGCTCTCCAATACTGGTCAAGACACCATTCTCAAATGGAAGAAAGATTAGGAAATA
CGTCCCAAGAGTTGCAATTNTCAAGTCCAGAATATAAAGCTTGCAGGAAGTNTGCAGCAT
GTGGCTGAAAAACTCTGCGTGAGCTGTATAACAAAGCTGGAGGAACCTTGAAGGAGGGCAA
AGTNTCCTCATNTACTATACACACACCACTTCCC

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FIGURE 232

GCCGAGCGCAAGAACCCCTGCGCAGCCCCAGAGCAGCTGCTGGAGGGGAATCGAGGCGCGGCTC
 CGGGGATTCGGCTCGGCGCTGGCTCTGCTCTGCGGGAGGGAGCAGGGCCCGCCCGCGGG
 CCCGAGCCCTCCGGATCCGCCCCCTCCCGGTCCCGCCCCCTCGGAGACTCCTCTGGCTGCT
 CTGGGGGTTCGCCGGGGCGGGGACCGCGGTCCGGGCGCC**ATG**CGGGCATCGCTGCTGCTG
 TCGGTGCTGGGCCCGCAGGGCCGTGGCGATCTCCCTGGGCTTCACCTGAGCCT
 GCTCAGCGTACCTGGGTGGAGGGAGCCGTGCGGCCAGGCCGCCAACCTGGAGACTCTG
 AGCTGCCGCGCGCAACACCAACGCCGCGCGCCGCCAACCTCGGTGAGGCCGAGCG
 GAGCGCAGAGGCCGGGGCGCGAAGGCGCCGGGAGAATTGGGAGCCGCGCTTGGC
 CTACCAACCTGCACAGGCCGCCAGGCCAAAAAGGCCGTCAAGGACCCGCTACATCAGCA
 CGGAGCTGGCATCAGGCAGAGGCTGCTGGTGGCGTGAACCTCTCAGACCAACGCTGCC
 ACGCTGGGCGTGGCGTGAACCGCACGCTGGGCACCGGCTGGAGCGTGTGGTGTTCCTGAC
 GGGCGCACGGGCCGCCGGGCCCCACCTGGCATGGCAGTGGCAGTGGTGAACGCTGGCGAGCGAC
 CCATTGGACACCTGCACCTGGCGTGCGCCACCTGCTGGAGCAGCACGGCGACGACTTTGAC
 TGGTCTCTGGTGCCTGACACCACCTACCGAGGGCGCACGGCTGGCACGCTTAACGG
 CCACCTCAGGCTGGCCTCCGCCGCCACCTGTACCTGGGCCGGGCCCCCAGGACTTCATGGCG
 GAGAGCCCACCCCCGGCGCTACTGCCACGGAGGCTTGGGTGCTGCTGCGCATGCTG
 CTGCAACAACTGCGCCCCACCTGGAAGGCTGCCCAACGACATCGTCACTGGTGA
 CGAGTGGCTGGTGGCTGCATTCTGATGCCACCGGGGTGGCTGACTGGTGAACACGAGG
 GGGTGCACTATAGCCATCTGGAGCTGAGCCCTGGGGAGCCAGTGCAGGAGGGGACCTCAT
 TTCCGAAGTGCCTGACAGGCCACCCCTGTGCGTGAACCTGTGCACATGTCACAGCTGCACAA
 AGCTTCGCCGAGCTGAACCTGGAACCGCACGTACCAAGGAGATCCAGGAGTTACAGTGGAGA
 TCCAGAATACCAACGCCATCTGGCCGTGATGGGACCGGGAGCTGCTTGGCCGTGGGTATT
 CCAGCACCATCCGCCGGCTCCCGCTTGAGGCTGCGTGCCTGACGGACTACTCACGGAGCA
 GCACGCTTCTGCGCCGATGGCTGCCACTGGCAGCTGCCACTGCGTGGGCTGACCGGGCTG
 ATGTGGCCGATGTTCTGGGACAGCTCTAGAGGAGCTGAACCGCCGCTACCACCGGCCCTG
 CGGCTCCAGAAGCAGCAGCTGGTAATGGCTACCGACGCTTGTATCCGGCCGGGTATGGA
 ATACACGCTGGACTTGCAGCTGGAGGCAGTGAACCCCCCAGGGAGGCCGGCCCTCACTC
 GCCGAGTGCAGCTGCTCCGCCGCTGAGCCGCGTGGAGATCTGCGCTGTGCCCTATGTCACT
 GAGGCCTACGTCTCACTGTGCTGCGCTTAGCTGCGTGAACGCTGACCTGGCCCTGG
 CTTCTGGAGGCCCTTGCCACTGCGCAGCTGGAGCCCTGGTGTATGCTGCGCAGCCCTGACCC
 TGCTGCTACTGTATGAGCCGCCAGGCCAGCGCGTGGCCATGCACTGCTTCGACCT
 GTCAAGGCCACGTGGCAGAGCTGGAGCGCGTTCCCGGTGCCATGGCTCAG
 TGTGCAGACAGCCGACCCCTACCAACTGCGCTCATGGATCTACTCTCCAAGAACGACCC
 TGGACACACTGTTCTGCTGGCCGGCCAGACACGGTGCTACGCGTACTTCTGAACCC
 TGCCGATGCATGCCATCTCCGGCTGGCAGGCCCTTCTTCCCATGCAATTCCAAGCCTCA
 CCCAGGTGGCCCCACCAAGGGCTGGGCCAGAGCTGGCCGTGACACTGGCGCT
 TTGATGCCAGGCAGCCAGCGAGGCCTGCTTCTACAAACTCCGACTACGTGGCAGCCGTGG
 CGCCTGGCGCAGCCTCAGAACAAAGAGGAGCTGGAGAGCCTGGATGTACGAGCT
 GTTCCCTCACTCTCCAGTCTGCATGTGCTGCGGGCGTGGAGGCCGGCTGCTGCAGCGCT
 ACCGGGCCAGACGTGCAGCGCGAGGCTAGTGAGGACCTGTACCAACCGCTGCCCTCAGAGC
 GTGCTTGAGGGCTCGGCTCCCGAACCCAGCTGGCCATGCTACTCTTGAACAGGAGCAGGG
 CAACAGCAC**TGA**ACCCACCCCTGCCCCGTGGCATGGCCACACCCACCCACTT
 CTCCCCAAAACCAGAGCCACCTGCCAGGCCCTGCTGGGAGGGCTGGCCGTAGCCAGACCC
 AAGCTGGCCACTGGTCCCCTCTGGCTCTGGCTCTGGTCCCTGGCTCTGGACAAGCACTGGG
 GGACGTGCCAGGCCAGAGCCACCCACTTCTCATCCAAACCCAGTTCCCTGCCCTGACGCT
 GCTGATTGGCTGTGGCCTCACGTATTATGCACTGAGTACGCTGCGCTGACGCCAGCCCTGC
 CTCGGCCCTGGGGCTGGCTGTAGAAGAGTTGGTGGGAAGGGAGGAGCTGAGGAGGG
 GCATCTCCAACTTCTCCCTTTGGACCCCTGCCGAAGCTCCCTGCCTTAATAAACTGGCCA
 AGTGTGGAAAAA

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FIGURE 233

MRASLLSVLRPAGPVAVGISLGFTLSLLSVTWVEPCGPQPGDSELPPRGNTNAARRP
NSVQPGAEERKPGAGEGAGENWEPRVLPYHPAQPGQAAKKAVRTRYISTELGIRQRLLAVL
TSQTLPTLGVAVNRTLGHRLERVVFLTGARGRRAPPMAVVTLGEERPIGHLHLALRHLE
QHGDDFDWFFLVPDTTYTEAHGLARLTGHLSASAALYLGRCQDFIGGEPTPGRYCHGGFG
VLLSRMLLQQQLRPHLEGCRNDIVSARPDEWLGRCIILDATGVGCTGDHEGVHYSHELSPGEP
VQEGDPHFRSALTAHPVRDPVHMYQLHKAFARAEERTYQEIQELQWEIQNTSHLAVGDRA
AAWPVGIPAPSRRPASRFEVLRWDYFTEQHAFSCADGSPRCPLRGADRADVADVLGTALEELN
RRYHPALRLQKQQLVNGYRRFDPARGMEYTLDLQLEALTPQGGRRPLTRRVQLLRPLSRVEI
LPVPYVTEASRLTVLLPLAAAERDLAPGFLEAFATAALEPGDAAAALTLLLYEPRQAQRVA
HADVFAVKAHVAELERRFPGARVPWLSVQTAAPSPRLMDLLSKHPLDTLFLLAGPDTVL
TPDFLNRCRMHAISGWQAFFPMHFQAFHPGVAPPQPGPPELGRDTGRFDRQAASEACFYNS
DYVAARGRLAAASEQEEELLESLDVYELFLHFSSLHVLRAVEPALLQRYRAQTCSARLSEDL
YHRCCLQSVLEGLGSRTQLAMLLFEQEQQNST

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FIGURE 234

GCTCTGGCCGGCCCCGGCGATTGGTCACCGCCCCTAGGGACAGCCCTGGCCTCCTGTAT
TGGCAAGCGCTGGCCACCTCCCCACACCCCTTGCAGCCTCCCTAGTGGAGAAAAGGAGT
AGCTATTAGCCAATTGGCAGGGCCCGCTTTAGAAGCTTGATTCCCTTGAAGATGAAAG
ACTAGCGGAAGCTCTGCCTCTTCCCCAGTGGCGAGGGAACTCGGGCGATTGGCTGGAA
CTGTATCCACCCAAATGTCACCGATTCTCCTATGCAGGAAATGAGCAGACCCATCAATAA
GAAATTCTCAGCCTGGCGAAAATGGTGGCCCCACGAAGCCACGACAACGGAGGCAAAG
AGGGTTGCTCAACGCCCGCCTCATTGGAAAACCAAATCAGATCTGGACCTATATAGCGTG
GCGGAGGCAGGGCGATGATTGTCGCGCTCGCACCCACTGCAGCTGCGCACAGTCGCAATTCT
TTCCCCGCCCTGAGACCCCTGCAGCACCATCTGTCATGGCGCTGGCTGTTGGTTGAGC
GCTCGCGTCTTGGCGCAGCGCGACGCGAGGGCTCCGGCCCGCGTCCGCTGGGA
ATCTAGCTTCTCCAGGACTGTGGTCGCCCCGTCCGCTGTGGCGGGAAAGCGGCCCCAGAAC
CGACCACACCGTGGCAAGAGGACCCAGAACCGAGGACGAAAATTGTATGAGAAGAACCA
GACTCCCATGGTTATGACAAGGACCCGTTGGACGTCTGGAACATGCGACTTGTCTTCTT
CTTGCGTCTCCATCATCCTGGCCTTGGCAGCACCTTGCGCTATCTGCGTACTACA
GGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCTTGTGAAATACCGAGAGGCCAATGGC
CTTCCCCATCATGGAATCCAATGCTTCGACCCAGCAAGATCCAGCTGCCAGAGGATGAGTG
ACCAGTTGCTAAGTGGGCTCAAGAAGCACCGCCTCCCCACCCCTGCCTGCCATTCTGAC
CTCTTCTCAGAGCACCTAATTAAAGGGCTGAAAGTCTGAA

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FIGURE 235

MAAGLFGLSARRLLAAAATRGLPAARVRWESSFSRTVVAPSAGKRPPEPTTPWQEDPEPE
DENLYEKNPDSHGYDKDPVLDVWNMRLVFFFGVSIILVLGSTFVAYLPDYRMKEWSRREAER
LVKYREANGLPIMESNCFDPSKIQLPEDE

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FIGURE 236

GGCGGGCTGGGCTGTTGGTTGAGCGCTGCCGTCTTGGCGGCAGCGCGACGCGAGGGC
TCCC GGCCGCCCGCGTCCGCTGGGAATCTAGCTTCTCCAGGACTGTGGTCGCCCGTCCGCT
GTGGCGGGAAAGCGGCCCCAGAACCGACCACACCGTGGCAAGAGGACCCAGAACCCGAGGA
CGAAAACTTGTATGAGAAGAACCCAGACTCCCATGGTTATGACAAGGACCCGTTTGGACG
TCTGGAACATGCGACTTGTCTTCTTGGCGTCTCCATCATCCTGGTCCTTGGCAGCACC
TTTGTGGCCTATCTGCCTGACTACAGGATGAAAGAGTGGTCCCGCCGCGAAGCTGAGAGGCT
TGTGAAATACCGAGAGGCCAATGGCCTTCCATCATGGAATCCAATGCTTCGACCCAGCA
AGATCCAG

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FIGURE 237

GGGGCGGCT**ATG**CCGCTTGCTCTGCTCGCCTGTTGCTCCTGGGGCCCGGCGGCTGGTGCGCT
TGCAGAACCCCCACGCGACAGCCTGCGGGAGGAACCTGTATCACCCCGCTGCCTTCCGGGG
ACGTAGCCGCCACATTCCAGTTCCGCACCGCCTGGGATTGAGCTTCAGCGGGAGGAGTG
TCCCATTACAGGCTCTTCCAAAGCCCTGGGCAGCTGATCTCAAGTATTCTACGGGA
GCTGCACCTGTCAATTACACAAAGGCTTGGAGGACCCGATACTGGGGCCACCCCTCTGC
AGGCCCCATCAGGTGCAGAGCTGTGGGCTGGTCCAAGACACTGTCACTGATGTGGATAAA
TCTTGAAGGAGCTCAGTAATGTCCTCTCAGGGATCTTCTGCGCCTCTCAACTCATCGA
CTCCACCAACACAGTCACTCCCACGCTGCCTCCTCAAACCCCTGGGCTGGCCAATGACACTG
ACCACTACTTCTGCGCTATGCTGTGCTGCCGGAGGTGGTCTGCACCGAAAACCTCACC
CCCTGGAAGAAGCTCTGCCCTGTAGTCCAAGGCAGGCCTCTCTGTGCTGCTGAAGGCAGA
TCGCTTGTCCACACCAGCTACCAACTCCCAGGCAGTGCATATCCGCCCTGTTGCAGAAATG
CACGCTGACTAGCATCTCCTGGGAGCTGAGGCAGACCCCTGTCAAGTTGATTCATGCCCTC
ATCACGGGGCAGGGAAAGAAAGACTGGTCCCTCTTCCGGATGTTCTCCGAACCCCTACCGA
GCCCTGCCCTGGCTTCAGAGAGCCGAGTCTATGTGGACATCACCACCTACAACCAGGACA
ACGAGACATTAGAGGTGCACCCACCCCCGACCACTACATATCAGGACGTATCCTAGGACT
CGGAAGACCTATGCCATCTATGACTTGCTGACACCGCCATGATCAACAACCTCGAAACCT
CAACATCCAGCTCAAGTGAAGAGACCCCCAGAGAATGAGGGCCCCCAGTGCCCTCTGC
ATGCCCAGCGGTACGTGAGTGGCTATGGGCTGCAGAAGGGGAGCTGAGCACACTGCTGTAC
AACACCCACCCATACCGGGCCTCCGGTGTGCTGGACACCGTACCCCTGGTATCTGCG
GCTGTATGTGACACCCCTCACCATCACCTCCAAGGGCAAGGGAGAACAAACCAAGTTACATCC
ACTACCAGCCTGCCAGGACCGGGCTGCAACCCACCTCCTGGAGATGCTGATTCACTGCG
GCCAACTCAGTCACCAAGGTTCCATCCAGTTGAGCGGGCGCTGCTGAAGTGGACCGAGTA
CACGCCAGATCCTAACCATGGCTTCTATGTCAGCCCATCTGCTCCTCAGGCCCTGTGCCA
GCATGGTAGCAGCCAAGCCAGTGGACTGGGAAGAGAGTCCCTCTTCAACAGCCTGTTCCA
GTCTCTGATGGCTCTAACTACTTGTGCGGCTCTACACGGAGCCGCTGCTGGTGAACCTGCC
GACACCGGACTTCAGCATGCCCTACAACGTGATCTGCCCTACGTGCACTGTGGTGGCGTGT
GCTACGGCTCTTCTACAATCTCTCACCCGAACCTTCCACATCGAGGAGCCCCGACAGGT
GGCCTGGCCAAGCGGCTGGCCAACCTTATCCGGCGCCCGAGGTGTCCTCCCCCACTC**TGATT**
CTTGCCTTCCAGCAGCTGCAGCTGCCCTCTCTGGGAGGGAGGCCAAGGGCTTT
TCTGCCACTGCTCTCCTCAGAGTTGGCTTGAACCAAAGTGCCTGGACCAGGTCAAGGGC
CTACAGCTGTGTTCCAGTACAGGAGCACGAGCCAATGTGGCATTGAATTGAATTAA
CTTAGAAATTCAATTCCACCTGTAGTGGCCACCTCTATATTGAGGTGCTCAATAAGCAA
AGTGGTCGGTGGCTGCTGTTGGACAGCACAGAAAAAGATTCCATACCAAGAGAAAGGTG
GGCTGGCAGCACTGGCCAAGGTGATGGGTGTGCTACACAGTGTATGTCAGTGTGAGTGG
TGGAGTTACTGTTGTGGAATAAAACGGCTGTTCCGTGGAAAAAAAAAAAAAA

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FIGURE 238

MPLALLVLLLLGPGGWCLAEPPRDSLREELVITPLPSGDVAATFQFRTRWDSELQREGVSHY
RLFPKALGQLISKYSLRELHLSFTQGFWRTRYWGPPFLQAPSGAELWVWFQDTVDVDKSWK
ELSNVLSGIFCASLNFIDSTNTVTPTASFKPLGLANDTDHYFLRYAVLPREVVCTENLTPWK
KLLPCSSKAGLSVLLKADRLFHTSYHSQAVHIRPVCRNARCTSISWELRQTLSVVFDAFITG
QGKKDWSLFRMFSRTLTERCPLASESRVYVDITTYNQDNETLEVHPPPTTYQDVILGTRKT
YAIYDLLDTAMINNSRNLNIQLKWRPPNEAPPVPFLHAQRYVSGYGLQKGELSTLLYNTH
PYRAFPVLLLDTPWYLRLYVHTLTITSKGKENKPSYIHYQPAQDRLQPHLLEMLIQLPANS
VTKVSIQFERALLKWTETYPDPMHGFYVSPSVLSALVPSMVAAKPVDWEESPLFNSLFPVSD
GSNYFVRLYTEPLLVNLPTPDFSMPYNVICLTCTVVAVCYGSFYNLLRTFHIEPRTGGLA
KRLANLIRRARGVPPL

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FIGURE 239

CAACATGGGGTCCAGCAGCTTCTTGGTCCTCATGGTGTCTCTCGTTCTGTGACCCCTGGTGG
CTGTGGAAGGAGTTAAAGAGGGTATAGAGAAAGCAGGGTTGCCAGCTGACAACGTACGC
TGCTTCAAGTCCGATCCTCCCCAGTGTACACAGACCAGGACTGTCTGGGGAAAGGAAGTG
TTGTTACCTGCACTGTGGCTTCAAGTGTGATTCTGTGAAGGAACTGGAAGAAGGAGGAA
ACAAGGATGAAGATGTGTCAAGGCCATACCCCTGAGCCAGGATGGGAGGCCAAGTGTCCAGGC
TCCTCCTCTACCAGGTGTCCTCAGAAATGATGCTGGGTCTTCTACCTCTGGGGTCACTC
TCACTTGGCACCTGCCCTGAGGGCCTGAGACTTGGAAATATGGAAGAAGCAATACCCAAACC
CCACCAAAGAAAACCTGAGCTTGAAGTCCTTTCCCCAAAAAGAGGGAAAGAGTCACAAAAAG
TCCAGACCCCAGGGACGGTACTTCCCTCTACCTGGTGCCTCCCTAATGCTCATGAAT
GGACCCCTCATGAATGAAACCAGTGCCTTATAAGAGACCCAAAGAGCTGCCTGCCCTC
TGCATGTGATCACAGCTAGAAGGCACTGTCAAGAGAAGAGAAACTGGTCCTCACCAGATG
CTGAATCTGCTGGTGCCTGATCTGGACTTCCAGCCTCTAGAACTGTAAGAAATAATAT
TTGCTGTTATAATCCAA

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FIGURE 240

MGSSSFLVLMVSLVLVTLVAVEGVKEGIEKAGVCPADNVRCFKSDPPQCHTDQDCLGERKCC
YLHCGFKCVIPVKELEEGGNKDEDVSRPYPEPGWEAKCPGSSSTRCPQK

Signal sequence:

amino acids 1-19

N-myristoylation sites:

amino acids 23-29, 27-33, 32-38, 102-108

WAP-type 'four-disulfide core' domain signature:

amino acids 49-63

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FIGURE 241

AAACTCAGCACTGCCGGAGTGGCTCATGTTAAGACAAAGGGTGTGCACCTCCTGGCCAGG
AAACCTGAGCGGTGAGACTCCCAGCTGCCTACATCAAGGCCAGGACATGCAGAACCTCC
TCTAGAACCGACCCACCACCATGAGGTCTGCCTGTGGAGATGCAGGCACCTGAGCCAAGG
CGTCCAGTGGCTCTGCTTCTGGCTGTCTGGTCTTCTTCCTGCCTGCCCTCTTTA
TTAAGGAGCCTCAAACAAAGCCTTCCAGGCATCAACGCACAGAGAACATAAAGAAAGGTCT
CTACAGTCCCTGGCAAAGCCTAAGTCCCAGGCACCCACAAGGGCAGGGAGGACAACCAC
TGCAGAGCCAGCGCCAGAGAACATGCCCTCAACACACAAACCCAGCCAAGGCCACACCA
CCGGAGACAGAGGAAAGGAGGCAACCAGGCACCGCCGGAGGAGCAGGACAAGGTGCCAC
ACAGCACAGAGGGCAGCAGTGGAGAGGCCAGAAAAAGAGAAAACCAGTGGTAACACACTGTC
ACCCAGAGGGCAAGATGCAGGGATGGCCTCTGGCAGGACAGAGGACAATCATGGAAGAGCC
AGGACACAAAGACGACCCAAGGAAATGGGGGCCAGACCAGGAAGCTGACGCCCTCCAGGACG
GTGTCAGAGAACGACCAAGGGCAAAGCGGAACCACAGCCAAGACGCTATTCCAAAAGTCA
GCACAGAATGCTGGCTCCCACAGGAGCAGTGTCAACAAGGACGAGACAGAAAGGAGTGA
CAGCAGTCATCCCACCTAAGGAGAACCTCAGGCCACCCACCCCTGCCCTTCCAG
AGCCCCACGACGCAGAGAACCAAAGACTGAAGGCCCAACTTCAAATCTGAGCCTGGTG
GGATTTGAGGAAAATACAGCTCGAAATAGGAGGCCTCAGACGACTGCCCTGACTCTG
TGAAGATCAAAGCCTCAAGTCGCTGTGGCTCAGAAACTCTTCTGCCAACCTCACTCTC
TTCTGGACTCCAGACACTTCAACCAGAGTGAAGTGGGACCGCCTGGAACACTTGCACCACC
CTTGGCTTCATGGAGCTCAACTACTCCTGGTGCAAGGTCGTGACACGCTCCCTCCAG
TGCCCCAGCAGCAGCTGCTCTGCCAGCCTCCCCCTGGAGCCTCCGGTCATCACCTGT
GCCGTGGTGGCAACGGGGCATCCTGAACAACACTCCCACATGGGCCAGGAGATAGACAGTCA
CGACTACGTGTTCCGATTGAGCGGAGCTCTCATAAAGGCTACGAACAGGATGTGGGACTC
GGACATCCTCTACGGCTTACGCCCTCTCCCTGACCCAGTCACCTTATATTGGCAAT
CGGGGTTCAAGAACGTGCCTTGGAGGACGTCCGCTACTGCACCTCCTGGAAGGCAC
CCGGGACTATGAGTGGCTGGAAGCACTGCTTATGAATCAGACGGTGATGTCAAAAACCTT
TCTGGTTCAAGGCACAGACCCCAGGAAGCTTCTGGGAAGGCCCTGCACATGGACAGGTACCTG
TTGCTGCACCCAGACTTCTCCGATACATGAAGAACAGTTCTGAGGTCTAAGACCTGGA
TGGTCCCACGGAGGATATACGCCACCAACTGGGCCCTCTGCTGCTCACTGCCCTC
AGCTCTGTGACCAGGTGAGTGCCTATGGCTTCATCACTGAGGGCCATGAGCGCTTTCTGAT
CACTACTATGATACATCATGGAAGCGGCTGATCTTACATAAACCATGACTCAAGCTGGA
GAGAGAAGTCTGGAAGCGGCTACAGATGAAGGGATAATCCGGCTGTACCGCGCTGGTC
CCGGAACTGCCAAAGCCAAGAACATGAGGGCTGCCATGGCTCCTGCCCTGCT
CAAGGCACAGGATACAGTGGGAATCTTGAGACTCTTGGCCATTCCCATGGCTCAGACTAA
GCTCCAAGCCCTTCAGGAGTTCCAAGGGAACACTTGAACCATGGACAAGACTCTCAAGAT
GGCAAATGGCTAATTGAGGTTCTGAAGTCTCAGTACATTGCTGTAGGTCTGGCCAGG
GATTTTAATTAAATGGGTGATGGGTGCCAATACCAAACTCCTGCTGAAACACTCTT
CCAGTCCAAAGCTCTTGATACAGAAAAAGAGCCTGGATTACAGAAACATATAGATCTG
GTTGAATTCCAGATCGAGTTACAGTTGAAATCTGAAGGTATTACTTAACCTCACTAC
AGATTGTCTAGAAGACCTTCTAGGAGTTATCTGATTCTAGAAGGGTCTATACTTGTCTTG
TCTTAAGCTATTGACAACCTACGTGTTGAGAAAAGTATAAAACAAATGATTGTT
GTCCATGGAAAGGCAAATAAATTCTACAGTGAaaaaaaaaaaaa

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FIGURE 242

MRSCLWRCRHLSQGVQWSLLLAVLVFFLALPSFIKEPQTKPSRHQRTENIKERSLQSLAKP
KSQAPTRARRTTIYAEPAPENNALTQTPKAHTTGDRGKEANQAPPEEQDKVPHTAQRAAW
KSPEKEKTMVNTLSPRGQDAGMASGRTEAQSWKSQDTKTTQGNGGQTRKLTASRTVSEKHQG
KAATTAKTLIPKSQHRLAPTGAVSTRTRQKGVTAVIPPKEKKPQATPPPAPFQSPTTQRN
QRLKAANFKSEPRWDFFEEKYSFEIGGLQTTCPDSVKIKASKSLWLQKLFPLPNLTFLDSRHF
NQSEWDRLEHFAPPFGFMELNYSLVQKVVFTRFPVPQQQLLLASLPAGSLRCITCAVVGNGG
ILNNSHMGQEIDSHDYVFRSGALIKGYEQDVGTRTSFYGFTAFSLTQSLLILGNRGFKNVP
LGKDVRYLHFLEGTRDYEWLEALLMNQTVMSKNLFWFRHRPQEAFREALHMDRYLLLHPDFL
RYMKNRFLRSKTLGDAHWRIYRPTTGALLLTALLCDQVSAYGFITEGHERFSDHYYDTSW
KRLIFYINHDFKLEREVWKRLHDEGIIRLYQRPGPGTAKAKN

Cytoplasmic Domain:

amino acids 1-10

Type II Transmembrane Domain:

amino acids 11-35

Lumenal catalytic Domain:

amino acids 36-600

Ribonucleotide Reductase small subunit Signature:

amino acids 481-496

N-glycosylation Sites:

amino acids 300-303, 311-314, 331-334, 375-378, 460-463

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FIGURE 243

CGATGCGCGGACCCGGGCACCCCTCCTGGGGCTGCTGCTGGTGC
GAGCAGCGAGTGGAAATTGTTCTCGAGATCTGAGGATGAAGGACAAGTTCTAAAACACCT
TACAGGCCCTTTATTTAGTCCAAAGTCAGCAAACACTCCATAGACTTATCACAACA
CCAGAGACTGCACCATTCTGCATACTATAAAAGATGCGCCAGGCTTACCCGGCTGGCT
GTCAGTCCAGTGTGCATGGAGGATAAGTGAGCAGACCGTACAGGAGCAGCACACCAGGAGCC
ATGAGAAGTGCCTGGAAACCAACAGGGAAACAGAACTATCTTATACACATCCCTCATGG
ACAAGAGATTATTTGCAGACAGACTCTCCATAAGTCCTTGAGTTGTATGTTGTTG
ACAGTTGCAGATATATATTCGATAAATCAGTGTACTGACAGTGTATCTGTCACTTATT

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FIGURE 244

MRGPGHPLLGLLLVLGPSPEQRVEIVPRDLRMKDCKFLKHLTGPLYFSPKCSKHFHRLYHNT
RDCTIPAYYKRCARLLTRLAVSPVCMEDK

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FIGURE 245

GGGCTGGGCCCGCCGCAGCTCCAGCTGGCCGGCTTGGTCCTGCGGTCCCTCTGGGAGG
CCCGACCCCGGCCGCCAGCCCCCACCATGCCACCCGCCGGCTCCGCCGGGCCGCC
CTCACCGCAATCGCTCTGGTGGCTGGGGCTCCCTGGTGTGGCCGGCGAGGACTGCCT
GTGGTACCTGGACCGGAATGGCTCCTGGCATCGGGGTTAAGTGCAGTTCTCACCTCT
GCTGCGGGACCTGCTACCATCGGTACTGCTGCAGGGACCTGACCTGCTTATCACCGAGAGG
CAGCAGAACGACTGCCTGGCCTCAGCCCCAAGACCATAGCAGGCATGCCTCAGCTGTGAT
CCTCTTGTGCTGTGGTGCACCACCATCTGCTGCTTCCTGTTCCTGTTGCTACCTGT
ACCGCCGGGCCAGCAGCTCCAGAGCCCATTGAAGGCCAGGAGATTCCAATGACAGGCATC
CCAGTGCAGCCAGTATACCCATACCCCCAGGACCCAAAGCTGGCCCTGCACCCCCACAGCC
TGGCTTCATGTACCCACCTAGTGGTCCTGCTCCCCAATATCCACTCTACCCAGCTGGGCC
CAGTCTACAACCCCTGCAGCTCCCTCCCTATATGCCACACAGCCCTTACCCGGGAGCC
TGAGGAACCAGCCATGTCTCTGCTGCCCTTCAGTGATGCCAACCTGGGAGATGCCCTCAT
CCTGTACCTGCATCTGGCCTGGGGTGGCAGGAGTCCTCCAGCCACCAGGCCAGACCAA
GCCAAGCCCTGGGCCCTACTGGGACAGAGCCCCAGGAAGTGGAACAGGAGCTGAACAGA
ACTATGAGGGGTTGGGGGAGGGCTTGAATTATGGGCTATTTTACTGGGGCAAGGGAGG
GAGATGACAGCCTGGTCACAGTGCCTGTTCAAATAGTCCCTGCTCCAAAGATCCCAG
CCAGGAAGGCTGGGCCCTACTGTTGTCCTCTGGCTGGGTGGGGAGGGAGGGAGG
TCCGTCAGCAGCTGGCAGTAGCCCTCTCTGGCTGCCCACTGGCACATCTGGCCTG
CTAGATTAAGCTGTAAAGACAAAA

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FIGURE 246

MPPAGLRRAAPLTAIALLVLGAPLVLAGEDCLWYLDRNGSWHPGFNCEFFTFC CGTCYHRYC
CRDLTLLITERQQKHCLAFSPKTIAGIASAVILFVAVVATTICCFLCSCCYLYRRRQQLQSP
FEGQEIPMTGIPVQPVYPYPQDPKAGPAPPQPGFMYPPSGPAPQYPLYPAGPPVYNPAAPPP
YMPQQPSYPPGA

Transmembrane Domains:

amino acids 10-28, 85-110

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N-glycosylation Site:

amino acids 38-41

N-myristoylation Sites:

amino acids 5-10, 88-93

FIGURE 247

GGGGGAGCTAGGCCGGCGCAGTGGTGGGGCGCGCAAGGGTGAGGGCGGCCAGAA
 CCCAGGTAGGTAGAGCAAGAAGATGGTGTCTGCCCTCAAATGGCCCTTGCACCATG
 TCATTTCTACTTTCTCACTGTGGCTCTTAACGTGTCACTCCTCATGGTGTAGAG
 CACTGAAGCATCTCCAAAACGTAGTGTGGACACCATTCTGGAAATAAACGACTTC
 CTGAGTACGTACATCCCAGTTCAATTGATCTTGTATGCCATGAAACCTTACACGCTGACC
 TTCTGGGAACCACGAAAGTAGAAATCACAGCAGTCAGGCCACCAGCACCATCATCCTGCA
 TAGTCACCACCTGCAGATATCTAGGGCCACCCCTCAGGAAGGGAGCTGGAGAGAGGCTATCGG
 AAGAACCCCTGCAGGTCTGGAACACCCCCCTCAGGAGCAAATTGCACTGCTGGCTCCCGAG
 CCCCTCTGTGGGGCTCCCGTACACAGTTGTCATTCACTATGCTGGCAATCTTCGGAGAC
 TTTCCACGGATTAAACAAAGCACCTACAGAACAGAAGGGAACTGAGGATACTAGCAT
 CAAACACAATTGAACCCACTGCAGCTAGAATGGCTTCCCTGCTTGTGATGAACCTGCCTTC
 AAAGCAAGTTCTCAATCAAAATTAGAAGAGGCAAGGCACCTAGCCATCTCAAATATGCC
 ATTGGTGAATCTGTACTGTGCTGAAGGACTCATAGAACGACATTGTGATGTCACTGTGA
 AGATGAGCACCTATCTGGTGGCCTCATCATTCAAGATTTGAGTCTGTCAAGAACGATAACC
 AAGAGTGGAGTCAGGTTCTGTTATGCTGTGCCAGACAAGATAATCAAGCAGATTATGC
 ACTGGATGCTGGTACTCTCTAGAATTATGAGGATTATTCAGCATACCGTATCCCC
 TACCCAAACAGATCTGCTGTATTCCGACTTTCACTGCTGGTCTATGGAAAACGGGGA
 CTGACAACATATAGAGAATCTGCTGTGTGGATGTCAGGAAAGTCTCTGCATCAAGTAA
 GCTGGCATCACAGTACTGTGGCCCATGAACACTGGCCACCAGTGGTTGGAACCTGGTCA
 CTATGGAATTGGGAATGATCTTGGCTAAATGAAGGATTGGCAAAATTATGGAGTTGTG
 TCTGTCAGTGTGACCCATCCTGAACACTGAAAGTTGGAGATTATTCCTGGCAAATGTTGA
 CGCAATGGAGGTAGATGTTAAATCCTCACACCCCTGTGCTACACCTGTGGAAAATCCTG
 CTCAGATCCGGGAGATGTTGATGATGTTCTTATGATAAGGGAGCTGTATTCTGAATATG
 CTAAGGGAGTATCTAGCGTGCACGCAATTAAAGTGGTATTGTACAGTATCTCCAGAACG
 TAGCTATAAAACACAGGACCTGTGGGATAGTATGGCAAGTATTGCCCTACAG
 ATGGTGTAAAAGGGATGGATGGCTTGTCTAGAAGTCACATTCTCATCCTCACAT
 TGGCATCAGGAAGGGGGTGGATGTAACACTGGACACTGCGAGAGGGTT
 TCCCCTAATAACCATCACAGTGAGGGGGAGGAATGACATGAAGAACAGACATAGA
 AGGGCTCTGACGGCGCCCGGACACTGGTACCTGTGGCATTTGACATCATTACACC
 AGCAAATCCAACATGGCCATCGATTTCGCTAAACAAAACAGATGTGCTCATCCTCCC
 AGAAGAGGTGAATGGATCAAATTAAATGTGGGATGAATGGCTATTACATTGTGCTTACG
 AGGATGATGGATGGACTCTTGACTGGCTTTAAAAGGAACACACAGCAGTCAGCAGT
 AATGATGGCAAGTCTCATTAACAATGCATTCACTGTCAGCATTGGGAAGCTGTCCAT
 TGAAAAGGCCCTGGATTATCCCTGTACTTGAACACTGAAATTATGCCCTGTTTC
 AAGGTTGATGAGCTGATTCTATGTTAAGTAAATGGAGAAAAGAGATATGAATGAAGTG
 GAAACTCAATTCAAGGCCCTCCTCATCAGGCTGCTAAGGGACCTATTGATAAGCAGACATG
 GACAGACGAGGGCTCAGTCTCAGACAAATGTCGCGAGTGAACACTACTCCTCGCCTGTG
 TGCACAACATCAGCCGTGCGTACAGAGGGCAGAAGGCTATTCAAGAAAGTGGAAAGGAATCC
 AATGGAAACTTGAGCCCTGCCGTGACGTGACCTGGCAGTGTGCTGGGGGCCAGAG
 CACAGAAGGCTGGGATTTCTTATGAAATATCAGTTCTTGTCCAGTACTGAGAAAA
 GCCAAATTGAATTGCCCTCTGCAGAACCCAAAATAAGGAAAAGCTCAATGGCTACTAGAT
 GAAAGCTTAAAGGGAGATAAAAATAAAACTCAGGAGTTCCACAAATTCTACACTCATGG
 CAGGAACCCAGTAGGATACCCACTGGCCTGGCAATTCTGAGGAAAAGCTGAACAAACTG
 TACAAAAGTTGAACTTGGCTCATCTCCATGCCACATGGTAATGGGTACAACAAATCAA
 TTCTCCACAAGAACACGGCTTGAAGAGGTTAAAGGATTCTCAGCTTTGAAAGAAAATGG
 TTCTCAGCTCCGGTGTGTCACAGACAATTGAAACCATTGAAAGAAAACATCGGGTGGATGG
 ATAAGAATTGATAAAATCAGAGTGTGGCTGCAAAGTGAAGGCTTGAACGTATGTAAAAA
 TTCCCTCCCTGCCGGTCTGTTATCTCTAATCAACATTGTTGAGTGTATTTCAA
 ACTAGAGATGGCTGTTGGCTCCAAGTGGAGATACTTTTCTTCAACTCATTTTGA
 CTATCCCTGTGAAAAGAATAGCTGTTAGTTTCACTGAATGGGCTTTTCACTGAATGGGCTA
 TCGCTACCATGTGTTGTTCACTCACAGGTGTGCCCTGCAACGTAAACCCAAGTGTGGGT
 TCCCTGCCACAGAACAGAATAAAAGTACCTTATTCTCAAAAAAAAAAAAAAA

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FIGURE 248

MVFLPLKWSLATMSFLLSSLLALLTVSTPSWCQSTEASPKRSDGTPFPWNKIRLPEYVIPVH
YDLLIHANLTTLTFWGTTKVEITASQPTSTIILHSHHLQISRATLRKGAGERLSEEPLQVLE
HPPQEIQIALLAPEPLLGVGLPYTVVIHYAGNLSETFHGFYKSTYRTKEGELRILASTQFEPTA
ARMAFPCFDEPAFKASFISIKIRREPRHLAISNMPLVKSVTVAEGLIEDHFDVTVKMSTYLVA
FIISDFESVSKITKSGVKVSVYAVPDKINQADYALDAAVTLEFYEDYFSIPYPLPKQDLAA
IPDFQSGAMENWGLTTYRESALLFDAEKSSASSKLGITVTVAHELHQWFGNLVTMEWWNDL
WLNEGFAKFMEFVSVSVTHPELKVGDYFFGKCFDAMEVDALNSSHPVSTPVENPAQIREMFD
DVSYDKGACILNMLREYLSADAFKSGIVQYLQKHSYKNTKNEDLWDSMASICPTDGVKGMDG
FCSRSQHSSSSSHWHQEGVDVKTMMNTWTLQRGFPLITITVRGRNVHMKQEHYMKGSDGAPD
TGYLWHVPLTFITSKSNMVHRFLLKTDTVLILPEEVEWIKFNVGMNGYYIVHYEDDGWDSL
TGLLKGTHTAVSSNDRASLINNAFQLVSIGKLSIEKALDLSSLYLKHETEIMPVFQGLNELIP
MYKLMEKRDNEVETQFKAFLIRLLRDLIDKQTWTDEGSVSEQMLRSELLLACVHNYQPCV
QRAEGYFRKWKESNGNLSPVDVTLAVFAVGAQSTEGWDFLYSKYQFSLSSTEKSQIEFALC
RTQNKEKLQWLIDESFKGDKIKTQEFPQILTIGRNPVGYPLAWQFLRKNWNKLVQKFELGS
SSIAHMVMGTTNQFSTRTRLEEVKGFFSSLKENGSQLRCVQQTIETIEENIGWMDKNFDKIR
VWLQSEKLERM

Signal peptide:

amino acids 1-34

N-glycosylation sites:

amino acids 70-74, 154-158, 414-418, 760-764, 901-905

Neutral zinc metallopeptidases, zinc-binding region signature:

amino acids 350-360

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FIGURE 249

CAGGCCACAGACGGGTCATGAGCGCGTATTACTGCTGGCCCTCCTGGGGTCATCCTCCCAC
TGCCAGGAGTGCAGGCCTGCTCTGCCAGTTGGACAGTTCAGCATGTGTGGAAGGTGTCC
GACCTACCCCGCAATGGACCCCTAAGAACACCAGCTGCGACAGCGGCTGGGTGCCAGGA
CACGTTGATGCTCATTGAGAGCGGACCCAAGTGAGCCTGGTCTCCAAGGGCTGCACGG
AGGCCAAGGACCAGGAGCCCCGCGTCACTGAGCACCGGATGGGCCCGGCCTCTCCCTGATC
TCCTACACCTTCGTGTGCCGCCAGGAGGACTTCTGCAACAACTCGTTAACCTCCCTCCGCT
TTGGGCCACAGCCCCCAGCAGACCCAGGATCCTGAGGTGCCAGTCTGCTTGTCTATGG
AAGGCTGTCTGGAGGGACAACAGAAGAGATCTGCCCAAGGGACCACACACTGTTATGAT
GGCCTCCTCAGGCTCAGGGAGGGCATCTTCTCCAATCTGAGAGTCCAGGGATGCATGCC
CCAGCCAGGTTGCAACCTGCTCAATGGACACAGGAAATTGGGCCGTGGTATGACTGAGA
ACTGCAATAGGAAAGATTTCTGACCTGTCACTGGGGACCACCAATTATGACACACCGAAAC
TTGGCTCAAGAACCCACTGATTGGACCACATCGAATACCGAGATGTGCGAGGTGGGCAGGT
GTGTCAGGAGACGCTGCTGCTCATAGATGTAGGACTCACATCAACCCCTGGTGGGACAAAG
GCTGCAGCACTGTTGGGCTCAAAATTCCCAGAACGACCACCATCCACTCAGCCCTCCTGG
GTGCTTGTGCCCTCCTATACCCACTTCTGCTCCTCGGACCTGTGCAATAGTGCCAGCAGCAG
CAGCGTTCTGCTGAACCTCCCTCCCTCAAGCTGCCCTGTCCCAGGAGACCGGCAGTGT
CTACCTGTGTGCAGCCCCTTGGAACCTGTTCAAGTGGCTCCCCCGAATGACCTGCCAGG
GGCGCCACTCATTGTTATGATGGGTACATTCATCTCTCAGGAGGTGGCTGTCCACCAAAAT
GAGCATTAGGGCTGCGTGGCCAACCTTCAGCTTGTGAACCACACCAGACAAATCG
GGATCTCTGCGCGTGAGAACGCGTATGTGCAAGCCTCTGCCTCTCAGCATGAGGGAGGT
GGGGCTGAGGGCCTGGAGTCTCACTGGGGGTGGGCTGGCACTGGCCCCAGCGCTGT
GTGGGGAGTGGTTGCCCTTCCTGCTTAACTCTATTACCCCCACGATTCTCACCGCTGCTGA
CCACCCACACTCAACCTCCCTGACCTCATAACCTAATGCCCTGGACACCAGATTCTTC
CCATTCTGTCCATGAATCATCTCCCCACACACAATCATTCATATCTACTCACCTAACAGCA
ACACTGGGGAGAGCCTGGAGCATCCGGACTGCCCTATGGGAGAGGGACGCTGGAGGAGTG
GCTGCATGTATCTGATAATACAGACCCCTGTCCTTCA

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FIGURE 250

MSAVLLLALLGFILPLPGVQALLCQFGTVQHVWKVSDLPRQWTPKNTCDSGLGCQDTLMLI
ESGPQVSLVLSKGCTEAKDQEPRVTEHRMGPGLSISYTFVCRQEDFCNNLVNSLPLWAPQP
PADPGSLRCPVCLSMEGCLEGTEEICPKGTTHCYDGLRLRGGGIFSNLRVQGCMPQPGCN
LLNGTQEIGPGMTENCNRKDFLTCHRGTTIMTHGNLAQEPTDWTTSNTEMCEVGQVCQETL
LLIDVGLTSTLVGTTKGCVGAQNSQKTTIHSAPPGVLVASYTHFCSSDLCNSASSSVLLN
SLPPQAAPVPGDRQCPTCVQPLGTCSSGSPRMTCPRGATHCYDGYIHLGGGLSTKMSIQGC
VAQPSSFLLNHTRQIGIFSAREKRDVQPPASQHEGGGAEGLESLTWGVGLALAPALWWGVVC
PSC

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FIGURE 251

GCGACGGGCAGGACGCCCGTCGCCTAGCGCGTGCAGGAGTTGGTGTCCCTGCCTGCGCT
CAGGATGAGGGGAATCTGGCCCTGGTGGCGTTCTAATCAGCCTGGCCTTCCTGTCAGTGCTG
CCATCTGGACATCCTCAGCCGGCTGGCGATGACGCCCTGCTCTGTGCAGATCCTCGTCCCTGG
CCTCAAAGGGATGCGGGAGAGAAGGGAGACAAAGGCGCCCCCGGACGGCCTGGAAGAGTCG
GCCCCACGGGAGAAAAGGAGACATGGGGACAAAGGACAGAAAGGCAGTGTGGTCGTACAT
GGAAAAATTGGTCCCATTGGCTCTAAAGGTGAGAAAGGAGATTCCGGTGACATAGGACCCCC
TGGTCCTAATGGAGAACCAAGGCCTCCCATGTGAGTGCAGCCAGCTGCCAAGGCCATGGGG
AGATGGACAACCAGGTCTCTCAGCTGACCAGCGAGCTCAAGTTCATCAAGAATGCTGTCGCC
GGTGTGCGCAGACGGAGAGCAAGATCTACCTGCTGGTGAAGGAGGAGAACGCGCTACGCGGA
CGCCCAAGCTGTCCGCCAGGGCCGCGGGGACGCTGAGCATGCCAAGGACGAGGCTGCCA
ATGGCCTGATGGCCGCATACCTGGCGCAAGCCGGCCTGGCCGTGTCTTCATGGCATCAAC
GACCTGGAGAAGGAGGGCGCCTCGTGTACTCTGACCACTCCCCCATGCGGACCTTCAACAA
GTGGCGCAGCGGTGAGCCAACAATGCCTACGACGAGGAGACTGCGTGGAGATGGTGGCCT
CGGGCGCTGGAACGACGTGGCCTGCCACACCACCATGTACTTCATGTGTGAGTTGACAAG
GAGAACAT**TGAGCCTCAGGCTGGGCTGCCATTGGGGCCCCACATGTCCCTGCAGGGTT**
GGCAGGGACAGAGCCCAGACCATGGTGCCAGCCAGGGAGCTGTCCCTGTGAAGGGTGGAG
GCTCACTGAGTAGAGGGCTGTTGTCTAAACTGAGAAAATGGCCTATGCTTAAGAGGAAAATG
AAAGTGTCTGGGTGCTGTCTGAAGAACAGAGTTTACCTGTATTGTAGCCCCA
ATGTCATTATGTAATTATTACCCAGAATTGCTCTCCATAAAGCTTGTGCCTTGTCCAAGC
TATACAATAAAATCTTAAGTAGTGCAGTAGTTAAGTCCAAAAAAAAAAAAAA

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FIGURE 252

MRGNLALVGVLISLAFSLPSGHQPAGDDACSVQILVPGLKGDAGEKGDKGAPGRPGRVG
PTGEKGDMGDKQKGKGSVGRHGKIGPIGSKGEKGDSGDIGPPGPNGEPGLPCECSQLRKAIGE
MDNQVSQLTSELKFIKNAVAGVRETESKIYLLVKEEKRYADAQLSCQGRGGTLSMPKDEAN
GLMAAYLAQAGLARVFIGINDLEKEGAFVYSDHSPMRTFNKWRSGEPNNAYDEEDCVERVAS
GGWNDVACHTTMYFMCEFDKENM

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FIGURE 253

AGTGACTGCAGCCTTCCTAGATCCCCTCCACTCGGTTCTCTCTTGCAGGAGCACCGGCAG
CACCACTGTGTGAGGGGAGCAGGCAGCGGTCTAGCCAGTCCCTGATCCTGCCAGACCACC
CAGCCCCGGCACAGAGCTGCTCCACAGGCACCATGAGGATCATGCTGCTATTCACAGCCAT
CCTGGCCTTCAGCCTAGCTCAGAGCTTGGGCTGTCTGTAAGGAGCCACAGGAGGAGGTGG
TTCCTGGCGGGGGCCGCAGCAAGAGGGATCCAGATCTCTACCAGCTGCTCCAGAGACTCTC
AAAAGCCACTCATCTCTGGAGGGATTGCTCAAAGCCCTGAGCCAGGCTAGCACAGATCCTAA
GGAATCAACATCTCCGAGAAACGTGACATGCATGACTTCTTGTGGACTTATGGCAAGA
GGAGCGTCCAGCCAGAGGGAAAGACAGGACCTTCTTACCTTCAGTGAGGGTTCCCTGGCCC
CTTCATCCAATCAGCTTGGATCCACAGGAAAGTCTTCCCTGGAACAGAGGAGCAGAGACC
TTTATAAAGACTCTCCTACGGATGTGAATCAAGAGAACGTCCCCAGCTTGGCATCCTCAAGT
ATCCCCCGAGAGCAGAACAGGAACTCCACTTCCGGACTCCTGGACTGCATTAGGAAGACCTC
TTTCCCTGTCCAATCCCCAGGTGCGCACGCTCCTGTTACCTTCTTCCCTGTTCTTGT
AACATTCTTGTGCTTGACTCCTCTCCATCTTCTACCTGACCCCTGGTGTGAAACTGCA
TAGTGAATATCCCCAACCCCAATGGCATTGACTGTAGAATACCCCTAGAGTTCTGTAGTGT
CCTACATTAATAATGTCTCTCTTCTCAACAATAAAGGATTTTGCATATGAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 254

MRIMLLFTAILAFSLAQSGAVCKEPQEEVPGGGRSKRDPDLYQLLQRLFKSHSSLEGLLK
ALSQASTDPKESTSPEKRDMDFFVGLMGKRSVQPEGKTGPFLPSVRVPRPLHPNQLGSTGK
SSLGTEEQRPL

Important features:

Signal peptide:

amino acids 1-18

Tyrosine kinase phosphorylation site.

amino acids 36-45

N-myristoylation site.

amino acids 33-39, 59-65

Amidation site.

amino acids 90-94

Leucine zipper pattern.

amino acids 43-65

Tachykinin family signature.

amino acids 86-92

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FIGURE 255

GGCGTCTCCGGCTGCTCCTATTGAGCTGTCTGCTCGCTGTGCCCGCTGTGCCCTGTGCC
CGCGCTGTCGCCGCTGCTACCGCGTCTGCTGGACCGCGGAGACGCCAGCGAGCTGGTGATTG
GAGCCCTGCGGAGAGCTCAAGCGCCAGCTCTGCCCAAGGAGGCCAGGCTGCCCTGAGTC
CCATAGTTGCTGCAGGAGTGGAGCCATGAGCTGCCCTGGTGGTGTCACTCCCTGGGGC
TGCTGTTCTGGTCTGCGGATCCAAGGCTACCTCCTGCCAACGTCACTCTTAGAGGAG
CTGCTCAGCAAATACCAGCACAAACGAGTCTCACTCCGGTCCGCAGAGCCATCCCCAGGGA
GGACAAGGAGGAGATCCTCATGCTGCACAACAAGCTTCGGGCCAGGTGCAGCCTCAGGCCT
CCAACATGGAGTACATGGTGAGCGCCGGCTCCGGCGCAGAGGCTGGCACCGGGGTGGGC
CTGGGCCACCAGCCTGCTCTGTTCCCCAGGCCAGCTCTGTTCCCCAGCCAGTGCCTGATGG
CTGGCTCAGGGTCTCCTCTGGCAGGGAGGATCCCGCTCTGTTCTGTTGTTGTTGTT
TTGAGACAGGGTCTCACTCTGCCACTGACGCTGGAGTGCAATGGCACAAATCGTCACTGCCCTG
AAACCTTAGACTCCGGGTTAACGATCCTGCTTCAGCCTCCAAAGTAGCTGGAACATACAG
GCATGCACCATGGTGCCAGCTAGATTTAAATTTTGAGATGGGGTCTGCTACGT
TGCCCAAGGCTGGTCTGAACTCCTAGGCTCAAGCAATCCTCCTGCCCTAGCCTCTCAAAGTG
CTAGGATTATAGGCATGAGTCACCCCTGCTGGCTCTGGCTCTGTTCTTAACATTCTGCCAAA
ACAACACACGTGGTTCCCTGTGCAGAGCCTGCCCTCGTTGCTCATGTCACCTTGGTAGC
TCCACTGGGAACACAGCTCTCAGCCTTCCCACCTGGAGGCAGAGTGGGGAGGGGCCAGGG
CTGGGCTTGCTGATGCTGATCTCAGCTGTGCCACACGCTAGCTGCACCACCCCTGACTTC
CTTAGCCCCTGAGCCTCACTTCCACTTGGAGAGTCCTCGCGTGGTGCATGACT
GTGAGATAAGTCGAGGCTGTGAAGGGCCGGCACAGACTGACCTGCCCTCCAAACCCCTAGG
CTTGCTAACCGGAAAGGAGCTAACGGTACAGAAGACAGCCAAGGTCAACCCCTCCGGT
GATTGTGATGGGTGTTCCAGGTGTGGTGGCGATGCTGCTACTTGACCCCAAGCTCCAGT
TGGAAACTTCCCTGGCTGGTTTCCAGAACACTACAGAGGAATGGACCACAGTCTTCCAGG
GTCCCTCCTCGTCCACCAACCAGGGAGCCTCCACCTGGCCATCCGTAGCTATGAATGGCTT
TTAACAAACCCACGTCCCAGCCTGGTAACATGGTAAAGCCCCGTCTACAAAAAAATC
CAAGTTAGCCGGCATGGTGGTGCACCTGTAGTCCCAGCTGCAGTGGACTGAGGTGGAG
GTGGAGGTGGGGGTGGGAGCTGAGGAAGGAGGATCGCTTGAGCCTGGGAAGTCGAGGCTGC
AGTGAGCTGAGATTGCACCACTGCACCTCCAGCCTGGTGACAGAGCAAGACCCCTGCTCAAAA

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FIGURE 256

MSCVLGGVIPLLLFLVCGSQGYLLPNVTLLEELLSKYQHNESHSRVRAIPREDKEEILML
HNKLRGQVQPQASNMEYMVSAGSGRRGWHRGWGLGHQPALFSQLCSPASACDGWLKVSSGR
GGSRLCSVLFVCFETGSHSATDAGVQWHNRHALKP

Important features:

Signal peptide:

amino acids 1-22

N-glycosylation site.

amino acids 27-31, 41-45

N-myristoylation site.

amino acids 126-132, 140-146

Amidation site.

amino acids 85-89

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FIGURE 257

AAGGAGAGGCCACCGGGACTTCAGTGTCTCCTCCATCCCAGGAGCGCAGTGGCCACTATGGG
GTCTGGGCTGCCCTTGTCTCCTCTTGACCCCTGGCAGCTCACATGGAACAGGGCCGG
GTATGACTTGCAACTGAAGCTGAAGGAGTCTTGACAAATTCCCTATGAGTCCAGC
TTCCTGGAATTGCTTGAAAAGCTCTGCCTCCTCCATCTCCCTCAGGGACCAGCGTCAC
CCTCCACCATGCAAGATCTAACACCATGTTGTCTGCAACACATTGACAGCCATTGAAGCCTG
TGTCTTCTGGCCCGGGCTTTGGGCGGGGATGCAGGAGGCAGGCCCGACCCTGTCTT
CAGCAGGCCCGACCCTCCTGAGTGGCAATAAAATTGGTATGCTG

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FIGURE 258

MGSGLPLVLLLTLLGSSHGTGPGMTLQLKLKESFLTNSSYESSFELLEKLCLLHLPSGTS
VTLHHARSQHHVVCNT

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FIGURE 259

AATTGTATCTGTGTAATGTTAAAACAAACGAAATAAAAGAAGGAAAAACTTCTGAGTT
CAAAAACAAACAGACTAGTACTCTAAAGAACTCTTAAAACAATTAACTGTTAGGATTGCAGT
TATGATTGGATATTATTAATTCTGTTCTGATGTGGGGTTCCACTGTGTTCTGTGC
TATTAATATTTACCATTCGAGCTTCATTCACTGTTGAAAATGAATGCTTAGTGGATCTG
TGCCTCTTACGCATATGTTACAAATTATCTGGAGTCCCTAATCAATGCAGAGTTCCCCTCCC
CTCCGATTGTTCTAAAT**ATT**GAAAGATGTCGTGCTGGAAAAAGGCATGTATTAAATCTG
TATGATTCTCAACCATCTTAGTTGGAAAGGTCCCTGAAAGCCAATGGAAATACTTTTTT
TTTCTTGGCACTAATCAAGTGAGTGTTACCTTCACTTAGTAGGATGTGTTACGCTA
GTAAAATAGAACCTGTGTTATTCTCAGGTATTTAGAAACAACAGCCATCATTATT
ATGTGTGTTCTTGGCTGTATTCAAAATTATATATTTGGGCTATCAAATATTACTTCAT
TCAATATAAATAACAATAGTAGAAGTTACTTAGATATGCTTCTAGTGCTTTCT
AGCCTATGTAAGACTACTTGTGTAATAGCCTTGAAATTACAGTACTGTCTCTACTA
TCTTCAGATTACTTGATTCAAATAACCAATTATGTTGTAATTGATATTAATAAAACCAGA
ATAAAAGTTCATATCTACCC

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FIGURE 260

MIGYYLILFLMWGSSTVFCVLLIFTIAEASFVENECLVDLCLLRICYKLSGVPNQCRVPLP
SDCSK

Important features:

Signal peptide:

amino acids 1-29

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FIGURE 261

GAGGATTTGCCACAGCAGCGGATAGAGCAGGAGAGCACCACCGGAGGCCCTTGAGACATCCTT
GAGAAGAGCCACAGCATAAGAGACTGCCCTGCTGGTGTTCAGGATGATGGTGGCCCTT
CGAGGAGCTCTGCATTGCTGGTCTGTCCTTGAGCTTCTGCCCGCCAGTGTAC
CCAGGACCCAGCCATGGTGCATTACATCTACAGCGCTTCAGTCTGGAGCAAGGGCTGG
AAAAATGTACCCAAGCAACGAGGGCATACATTCAAGAATTCCAAGAGTCTCAAAAATATA
TCTGTCACTGGAAAGATGTCAAGACTACACAAGTGAAGTACAAGAGTGCAGTGGTAACCTT
GGCACTGAGAGTGAACGTCGGCCAAACGGGAGATTGACTACATACAATACCTTCGAGAGGCTG
ACGAGTGCATCGTATCAGAGGACAAGACACTGGCAGAAATGTTGCTCAAGAAGCTGAAGAA
GAGAAAAAGATCCGGACTCTGCTGAATGCAAGCTGTGACAAACATGCTGATGGGCATAAGTC
TTTGAAGAATAGTGAAGAAGATGGACACACATGGCTCTGGATGAAAGATGCTGTCTATA
ACTCTCAAAGGTGTACTTATTAATTGGATCCAGAAACAAACACTGTTGGGAAATTGCAAAC
ATACGGGCATTATGGAGGATAACACCAAGCCAGCTCCCCGGAAGCAAATCTAACACTTTC
CTGGCAGGGAACAGGCCAAGTGAATCACAAAGGTTTCTATTTTCATAACCAAGCAACCTT
CTAAATGAGATAATCAAATAACCTGCAAGAGGAGCTGTGGAAGATGCAATGCTGCCA
GGAGGGTAGGCCGAGCATTGGTTACCGACTCCCCCTCAACTACATTGACCTGGCTGT
GGATGAGCATGGCTCTGGGCCATCCACTCTGGGCCAGGCACCCATAGCCATTGGTTCTCA
CAAAGATTGAGCCGGCACACTGGGAGTGGAGCATTATGGGATACCCATGCAAGGCCAG
GATGCTGAAGCCTATTCCCTCTGTGTGGGTTCTCTATGTGGTCTACAGTACTGGGGCAG
GGGCCCTCATCGCATACCTGCATCTATGATCCACTGGGCACTATCAGTGGAGGACTTGC
CCAACTTGTCTTCCCCAAGAGACCAAGAAGTCACTCCATGATCCATTACAACCCAGAGAT
AAGCAGCTCTATGCCCTGGAATGAAGGAACCAGATCATTACAAACTCCAGACAAAGAGAAA
GCTGCCTCTGAAGTAAATGCACTACAGCTGTGAGAAAGAGCACTGTGGCTTGGCAGCTGTC
TACAGGACAGTGGGCTATAGCCCCCTCACAAATATAGTATCCCTCTAATCACACAGGAAG
AGTGTGAGAAGTGGAAATACGTATGCCCTTCCAAATGTCAGTGCCTTAGGTATCTC
CAAGAGCTTAGATGAGAGCATATCATCAGGAAAGTTCACAAATGTCCATTACTCCCCAAA
CCTCCTGGCTCTCAAGGATGACCACATTCTGATAACAGCCTACTCAAGCCTTTGTTTACT
GCTCCCCAGCATTACTGTAACCTGCATCTCCCTCCCACAATTAGAGTTGTATGCCAGC
CCCTAAATTCAACCAGTGGCTTCTCTCCCTGGCCTTGCTGAAGCTCTCCCTCTTT
CAAATGTCTATTGATATTCTCCATTTCAGGAAACTAAATACTATTAAATTATTCTT
CTTTCTTTCTTTTTGAGACAAGGCTCACTATGTTGCCAGGCTGGTCTCAAACCTC
AGAGCTCAAGAGATCCTCTGCCTCAGCCTCTAACAGTACCTGGGATTACAGGCATGTGCCAC
CACACCTGGCTAAAGACTATTCTTATTGAGGTTAACCTCTATTCCCCTAGCCCTGTC
CTTCACTAAGCTGGTAGATGTAATAATAAAAGTGAAGAATATTAAACATTGAATATCGCTT
CCAGGTGTGGAGTGTGACATCATTGAATTCTCGTTCACCTTGTGAAACATGCACAAG
TCTTACAGCTGTCATTCTAGAGTTAGGTGAGTAACACAATTACAAAGTGAAGATAACAGC
TAGAAAATACTACAAATCCATAGTTTCCATTGCCCAAGGAAGCATCAAATACGTATGTT
TGTTCACCTACTCTTATAGTCATGCGTTCATCGTTCAGCCTAAAGATAATAGTCTGCTCC
TTAGCCAGTTTCTATGTCTGCACAAGACCTTCAATAGGCCTTCAAATGATAATTCTCC
AGAAAACCAGTCTAAGGGTGAGGACCCAACTCTAGCCTCTTGCTGCTGCTCTGT
TTCTCTTTCTGCTTAAATTCAATAAAAGTGACACTGAGCAAAAAAA

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FIGURE 262

MMVALRGASALLVLFLAAFLLPPPQCTQDPAMVHYIYQRFRVLEQGLEKCTQATRAYIQEFQE
FSKNISVMLGRCQTYTSEYKSAVGNLALRVERAQRREIDYIQYLREADECIVSEDKTLAEMLL
QEAEKKIRTLLNASCDNMLMGIKSLKIVKKMMDTHGSWMKDAVYNSPKVYLLIGSRNNNTV
WEFANIRAFMEDNTKPAPRKQILTLSWQGTGQVIYKGFLFFHNQATSNEIIKYNLQKRTVED
RMILLPGGVGRALVYQHSPSTYIDLAVDEHGLWAIHSGPGTHSHLVLTKIEPGTLGVEHSWDT
PCRSQDAEASFLLCGVLYVVYSTGGQGPHRITCIYDPLGTISEEDLPNLFFPKRPRSHSMIH
YNPRDKQLYAWNENQIIYKLQTKRKLPLK

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FIGURE 263

GGGCGCCCGCGTACTCACTAGCTGAGGTGGCAGTGGTCCACCAAC**ATG**GAGCTCTCGCAGA
TGTGGAGCTCATGGGGCTGTCGGTGTGCTTGGCTGCTGCCCTGATGGCGACGGCGCG
GTAGCGCGGGGGTGGCTGCGCGGGGGAGGGAGAGGAGCGGCCGGCCGCTGCCAAAAAGC
AAATGGATTCCACCTGACAAATCTCGGGATCCAAGAAGCAGAAACAATATCAGCGGATT
GGAAGGAGAAGCCTCAACAACACAACCTCACCCACCGCCTGGCTGCAGCTGAAGAGC
CACAGCGGGAAACATATCTGCATGGACTTAGCAGCAATGGAAATACCTGGCTACCTGTGC
AGATGATCGCACCATCCGCATCTGGAGCACCAAGGACTTCCTGCAGCGAGAGCACCGCAGCA
TGAGAGCCAACGTGGAGCTGGACCACGCCACCCCTGGTGCCTCAGCCCTGACTGCAGAGCC
TTCATCGCTGGCTGGCAACGGGGACACCCCTCCGTGTTCAAGATGACCAAGCGGGAGGA
TGGGGCTACACCTCACAGCCACCCAGAGGACTCCCTAAAGCACAAGGCGCTGTCA
TCGACATTGGCATTGCTAACACAGGGAAAGTTATCATGACTGCCTCCAGTGACACCAACTGTC
CTCATCTGGAGCCTGAAGGGTCAAGTGCCTACCATCAACACCAACAGATGAACAAACAC
ACACGCTGCTGTATCTCCCTGTCAGATTGTAAGCCTCGTGTGGCTCACCCAGATGTGA
AGGTTTGGGAAGTCTGCTTGGAAAGAAGGGGGAGTTCCAGGAGGTGGTGCAGGCCCTCGAA
CTAAAGGCCACTCCGGCTGTGCACTCGTTGCTTCTCCAACGACTCACGGAGGATGGC
TTCTGTCTCCAAGGATGGTACATGGAAACTGTGGGACACAGATGTGGAATAAGAAGAAGC
AGGACCCCTACTGCTGAAGACAGGCCGTTGAAGAGGCCGGTGCCGCCGTGCCG
CTGGCCCTCTCCCCAACGCCAGGTCTGGCTTGCCAGTGGCAGTAGTATTCATCTCA
CAATACCCGGGGGGCGAGAAGGAGGAGTGCTTGAGCGGGTCCATGGCAGTGATCGCCA
ACTTGCTCTTGACATCACTGGCGTTCTGGCCTCCTGTGGGACCGGGGGCGGTGCCGCTG
TTTCACAACACTCCTGGCCACCGAGCCATGGTGGAGGAGATGCAGGGCCACCTGAAGCGGGC
CTCCAACGAGAGCACCCGCCAGAGGCTGAGCAGCAGCTGACCCAGGCCAAGAGACCC
AGAGCCTGGTGCCTGAAGAAG**TGA**CTGGGAGGGCCCGCGCAGAGGATTGAGGAGGAG
GGATCTGGCCTCCTCATGGCACTGCTGCCATCTTCCCTCCAGGTGGAAGCCTTCAGAAGG
AGTCTCCTGGTTTCTTACTGGTGGCCCTGCTTCTTCCATTGAAACTACTCTTGTCTACTT
AGGTCTCTCTTCTTGCTGGCTGTGACTCCTCCCTGACTAGTGGCCAAGGTGCTTTCTC
CTCCCAGGCCAGTGGTGGAACTGTCCCCACCTGGCACTGAGGAGAATGGTAGAGAGGAG
AGGAGAGAGAGAGAGAATGTGATTTGGCCTTGTGGCAGCACATCCTCACACCCAAAGAAG
TTTGTAAATGTTCCAGAACACCTAGAGAACACCTGAGTACTAAGCAGCAGTTGCAAGGA
TGGGAGACTGGGATAGCTCCCATCACAGAACTGTGTTCCATCAAAAGACACTAAGGGATT
TCCTTCTGGCCTCAGTTCTATTGTAAGATGGAGAATAATCCTCTGTGAACCTTGCA
AAGATGATATGAGGCTAACAGAAATATCAAGTCCCCAGGTCTGGAAGAAAAGTAGAAAAGAGT
AGTACTATTGTCATGAAAGTGGTAAAGTGGAACCCAGTGCTGCTTGAACCA
TTAGAAACACATTCTGGAGAGCTGATATCTGTTAAGGAGACCTCTTCAAGTTCATCAAG
TTCATCAGATATTGAGTGCCCACCTGTGCCAAATAATGAGCTGGGATTTAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 264

MELSQMSELMGLSVLLGLLALMATAAVARGWLAGEERSGRPACQKANGFPPDKSSGSKKQK
QYQRIRKEKPQQHNFTHRLLAAALKSHSGNISCMDSSNGKYLATCADDRTIRIWSTKDFLQ
REHRSMRANVELDHATLVRFSPDCRAFIWVLANGDTLRVFKMTKREDGGYTFTATPEDFPKK
HKAPVIDIGIANTGKFIMTASSDTTVLIWSLKGQVLSTINTNQMNNTHAAVSPCGRFVASC
FTPDKVWVFCFGKKGEFQEVVRAFELKGHSAAVHSFAFSNDSRRMASVSKDGTWKLWDTDV
EYKKKQDPYLLKTGRFEEAAGAAPCRLALSPNAQVLALASGSSIHLYNTRRGEKEECFERVH
GECIANLSFDITGRFLASCGRDRAVRLFHNTPGHGRAMVEEMQGHLKRASNESTRQRLQQQLTQ
AQETLKSLGALKK

Important features:**Signal peptide:**

amino acids 1-25

N-glycosylation site.

amino acids 76-80, 92-96, 231-235, 289-293, 378-382, 421-425

Beta-transducin family Trp-Asp repeat protein.

amino acids 30-47, 105-118, 107-119, 203-216, 205-217, 296-308

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FIGURE 265

TGGCCTCCCCAGCTGCCAGGCACAAGGCTGAGCGGGAGGAAGCGAGAGGCATCTAAGCAGG
CAGTGTTCGCCTCACCCCAAGTGACCATTAGGAGAGGTGCCACGCGAGTCTCAATCATGCTCC
TCCTAGTAACTGTGTCTGACTGTGCTGTGATCACAGGGGCTGTGAGCGGGATGTCCAGTGT
GGGGCAGGCACCTGCTGTGCCATCAGCCTGTGGCTTCGAGGGCTGCCATGTGACCCCCGCT
GGGGCGGGAAAGGCAGGGAGTGCCACCCGGCAGCCACAAGGTCCCTCTTCAGGAAACGCA
AGCACCACACCTGTCCTTGCTTGCCAACCTGCTGTGCTCCAGGTTCCGGACGGCAGGTAC
CGCTGCTCCATGGACTTGAAGAACATCAATTTAGGCCTGCCTGGTCTCAGGATAACCA
CCATCCTTTCCTGAGCACAGCCTGGATTTATTCTGCCATGAAACCCAGCTCCATGAC
TCTCCCAGTCCCTACACTGACTACCCCTGATCTCTCTGTCTAGTACGCACATATGCACACAG
GCAGACATACTCCCACATGACATGGTCCCCAGGCTGCCCTGAGGATGTCACAGCTTGAGG
CTGTGGTGTGAAAGGTGCCAGGCCTGGTCTCTCCCTGCTCAGGCTGCCAGAGAGGTGGTA
AATGGCAGAAAGGACATTCCCCCTCCCCTCCCCAGGTGACCTGCTCTTTCTGGGCCCTG
CCCCCTCCCCACATGTATCCCTGGTCTGAATTAGACATTCTGGCACAGGCTTGGGT
GCATTGCTCAGAGTCCCAGGTCCCTGCCCTGACCTCAGGCCCTCACGTGAGGTCTGTGAGG
ACCAATTGTGGTAGTTCATCTCCCTCGATTGGTTAACCTCTAGTTCAGACCAAGAC
TCAAGATTGGCTCTTCCCAGAGGGCAGCAGACAGTCACCCCAAGGCAGGTGTAGGGAGCCA
GGGAGGCCAATCAGCCCCCTGAAGACTCTGGTCCCAGTCAGCCTGTGGCTGTGCCCTGTGA
CCTGTGACCTCTGCCAGAATTGTCATGCCCTGAGGCCCTCTTACCAACTTACCA
TAACCACTGAAGCCCCAATTCCCACAGCTTTCCATTAAAATGCAAATGGTGGTCAA
TCTAAATCTGATATTGACATATTAGAAGGCAATTAGGGTGTTCCTAAACAACCTCTTCCA
AGGATCAGCCTGAGAGCAGGTGGTACTTGAGGAGGGCAGTCCTCTGTCCAGATTGGGG
TGGGAGCAAGGGACAGGGAGCAGGGCAGGGCTGAAAGGGGACTGATTGACACCAGGGAGG
CAACTACACACCAACATGCTGGCTTTAGAATAAAAGCACCAACTGAAAAAA

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FIGURE 266

MRGATRVSIMLLVTVSDCAVITGACERDVQCGAGTCCAISLWLRGLRMCTPLGREGEECHP
GSHKVPFFRKHKHTCPCLPNLLCSRFPDGRYRCSDMLKNINF

Signal peptide:

amino acids 1-19

Tyrosine kinase phosphorylation site:

amino acids 88-95

N-myristoylation sites:

amino acids 33-39, 35-41, 46-52

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FIGURE 267

AGCGCCGGCGTCGGGCGGTAAAAGGCCGGCAGAAGGGAGGCACTTGAGAAATGTCTTC
CTCCAGGACCAAGTTCTCACCATGGGGATGTGGTCCATTGGTGCAGGAGCCCTGGGGC
TGCTGCCTTGGCATTGCTGCTGCCAACACAGACGTGTTCTGTCCAAGCCCCAGAAAGCGG
CCCTGGAGTACCTGGAGGATATAGACCTGAAAACACTGGAGAAGGAACCAAGGACTTCAAA
GCAAAGGAGCTATGGGAAAAAAATGGAGCTGTGATTATGGCCGTGCGGAGGCCAGGCTGTT
CCTCTGTCGAGAGGAAGCTGCGGATCTGTCCTCCCTGAAAAGCATGTTGGACCAGCTGGCG
TCCCCCTCATGCAGTGGTAAAGGAGCACATCAGGACTGAAGTGAAGGATTCCAGCCTTAT
TTCAAAGGAGAAATCTCCTGGATGAAAAGAAAAAGTTCTATGGTCCACAAAGGCCGAAGAT
GATGTTATGGGATTATCCGTCTGGAGTGTGGTACAACCTCTTCCGAGCCTGGAACGGAG
GCTTCTCTGAAACCTGGAAGGAGAAGGCTTCATCCTGGGGAGTTTGTGGTGGGATCA
GGAAAGCAGGGCATTCTCTTGAGCACCGAGAAAAGAATTGGAGACAAAGTAAACCTACT
TTCTGTTCTGGAAGCTGCTAAGATGATCAAACCACAGACTTGGCCTCAGAGAAAAAATGAT
TGTGTGAAACTGCCAGCTCAGGGATAACCAGGGACATTCACCTGTGTTATGGGATGTATT
GTTTCACTCGTGTCCCTAAGGAGTGAGAAACCCATTATACTCTACTCTCAGTATGGATTA
TTAATGTATTTAATATTCTGTTAGGCCACTAAGGCAAATAGCCCCAAACAAGACTGA
AAAAATCTGAAAACTAATGAGGATTATTAAGCTAAACCTGGAAATAGGAGGCTTAAA
TTGACTGCCAGGCTGGGTGCAGTGGCTCACACCTGTAATCCCAGCACTTGGGAGGCCAAGG
TGAGCAAGTCACTTGAGGTGGAGTTCGAGACCAGCCTGAGCAAATGGCGAAACCCGTC
TCTACTAAAAATACAAAATCACCCGGGTGTGGTGGCAGGCACCTGTAGTCCCAGCTACCCG
GGAGGCTGAGGCAGGAGAACACTTGAACCTGGGAGGTGGAGGTTGCGGTGAGCTGAGATCA
CACCACTGTATTCCAGCCTGGGTGACTGAGACTCTAACTAA

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FIGURE 268

MSFLQDPSFTMGMWSIGAGALGAAALALLANTDVFLSKPQKALEYLEIDIDLKTEKEPR
TFKAKELWEKNGAVIMAVRRPGCFLCREEAADLSSLKSMLDQLGVPLYAVVKEHIRTEVKDF
QPYFKGEIFLDEKKKFYGPQRRKMMFMGFIRLGWYNFFRAWNGGFSGNLEGEGFILGGVVF
VGSGKQGILLEHREKEFGDKVNLLSVLEAAKMIKPQTLASEKK

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FIGURE 269

ACGGACCGAGGGTTCGAGGGAGGGACACGGACCAGGAACCTGAGCTAGGTCAAAGACGCCG
GGCCAGGTGCCCGTCGCAGGTGCCCTGGCCGGAGATGCGGTAGGAGGGGCGAGCGCGAGA
AGCCCCCTCCTCGGCCTGCCAACCCGCCACCCAGCCCATGGCGAACCCGGGCTGGGCTG
CTTCTGGCGCTGGGCCTGCCGTTCTGCTGGCCCGCTGGGGCCGAGCCTGGGGCAAATACA
GACCACTTCTGCAAATGAGAATAGCACTGTTGCCTCATCCACCAGCTCCAGCTCCGATG
GCAACCTGCGTCCCGGAAGCCATCACTGCTATCATCGTGGTCTTCTCCCTTTGGCTGCCTTG
CTCCTGGCTGTGGGCTGGCACTGTTGGTGCAGCTTCGGGAGAAGCGGCAGACGGAGGG
CACCTACCGGCCAGTAGCGAGGAGCAGTTCTCCATGCAGCCGAGGCCGGCCCTCAGG
ACTCCAAGGAGACGGTGCAGGGCTGCCTGCCATCTAGGTCCCCTCTGCATCTGTCTCC
CTTCATTGCTGTGTGACCTGGGAAAGGCAGTGCCCTCTGGGCAGTCAGATCCACCCAG
TGCTTAATAGCAGGGAAGAAGGTACTTCAAAGACTCTGCCCTGAGGTCAAGAGAGGATGGG
GCTATTCACTTTATATTTATATAAAATTAGTAGTGAGATGTAAAAAAAAAAAAAAA

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FIGURE 270

MANPGLGLLLALGLPFLARWGRAWGQIQTTSANENSTVLPSSSTSSSDGNLRPEAITAIIV
VFSLLAALLLAVGLALLVRKLREKRQTEGTYRPSSEEQFSHAAEARAPQDSKETVQGCLPI

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FIGURE 271

AATATATCATCTATTTATCATTAAATCAATAATGTATTCTTTATTCCAATAAACATTTGGGTT
TTGGGATTTAATTTCAAACACAGCAGAATGACATTTCTGTCACTATTATTATTGTG
GTATGTGAAGCTATGGAGATCCAATTAGGAAGCAACACATTGGAGAATGGCTACTTCT
ATCAAGAAATAAGAGAACCAACAGTCAACCCACACAATCATCTTAGAAGACAGTGTGACTC
CTACCAAAGCTGTCAAAACCACAGGCAAGGGCATAGTTAAAGGACGGAATCTGACTCAAGA
GGGTTAATTCTGGTGCTGAAGCCTGGGCAGGGGTGTAAAGAAAAACACTTAGATTCAATG
ATTGTAATTAAGGCAAATACACATATTAGTATTACCTTAGTGTAAATGTATCCCTGTCAATA
TATACAATAAGGTGAAATTATAAGTACCCATGCAGTTGGCTGGACAGTTCTAAATTGGACT
TTATTAATTTAAAATCAGTAACTGATTATCACTGGCTATGTGCTTAGATCTACAGGAGA
TCATATAATTGATAACAATAAGAAAAGTGTCTCTCCCTTACAGAATTGACATTTAA
ATGCGATACAGTTAGAATAGGAAATGACATTAGAAAGGAAGAATGACAGGGAGAAAGGAA
AGAAGGGAAAATGTTGCCAAGGAAAAAA

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FIGURE 272

MTFFLSLLLLVCEAIWRSNSGSNTLENGYFLSRNKENHSQPTQSSLEDSVTPTKAVKTTGK
GIVKGRNLDSRGLILGAEAWGRGVKKNT

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FIGURE 273

GGCAGGAATAACTAGAGAGGAACA**ATGGGGTTATT**CAGAGGTTTGT~~TTT~~CCTCTAGTTCT
GTGCCTGCTGCACCAGTCAAATACTCCTTCATTAAGCTGAATAATAATGGCTTGAAAGATA
TTGTCATTGTTATAGATCCTAGTGTGCCAGAAGATGAAAAAATAATTGAACAAATAGAGGAT
ATGGTGACTACAGCTTCTACGTACCTGTTGAAGCCACAGAAAAAAGATTTTTCAAAA
TGTATCTATATTAACTCCTGAGAATTGGAAGGAAAATCCTCAGTACAAAAGGCCAAACATG
AAAACCATAAACATGCTGATGTTATAGTGCACCCACCTACACTCCCAGGTAGAGATGAACCA
TACACCAAGCAGTTCACAGAATGTGGAGAGAAAGGGCAATACTACATTCACTCACCCTGACCT
TCTACTTGGAAAAAAACAAAATGAATAATGGACCAACCCAGGCAACTGTTGTCCATGAGTGGG
CTCACCTCCGGTGGGAGGTGTTGATGAGTACAATGAAGATCAGCCTCTACCGTGCTAAG
TCAAAAAAAATCGAACAAAGGTGTTCCGCAAGGTATCTCGGTAGAAATAGAGTTATAA
GTGTCAGGGAGGCAGCTGCTTACTAGAGCATGCAGAATTGATTACAAACAAAATGTATG
GAAAAGATTGTCATTCTTCCTGATAAAAGTACAAACAGAAAAAGCATCCATAATGTTATG
CAAAGTATTGATTCTGTTGTAATTGTAACGAAAAACCCATAATCAAGAACGCTCAAG
CCTACAAAACATAAAGTGAATTAGAAGTACATGGGAGGTGATTAGCAATTCTGAGGATT
TTAAAAACACCATAACCCATGGTGACACCACCTCCACCTGCTTCTCATTGCTGAAGATC
AGTCAAAGAATTGTCAGTGTGTTCTGATAAGTCTGGAAGCATGGGGGTAAGGACCGCT
AAATCGAATGAATCAAGCAGCAAAACATTCTGCTGCAGACTGTTGAAAATGGATCCTGGG
TGGGGATGGTCACTTGATAGTACTGCCACTATTGTAATAAGCTAATCCAAATAAAAAGC
AGTGTGAAAGAACACACTCATGGCAGGATTACCTACATATCCTCTGGGAGGAACCTCAT
CTGCTCTGGAATTAAATATGCAATTTCAGGTGATTGGAGAGCTACATTCCAACTCGATGGAT
CCGAAGTACTGCTGCTGACTGATGGGAGGATAACACTGCAAGTTCTGTATTGATGAAGTG
AAACAAAGTGGGCCATTGTTATTGCTTGGGAAGAGCTGCTGATGAAGCAGTAAT
AGAGATGAGCAAGATAACAGGGAGGAAGTCATTGTTATGTTGAGATGAAGCTCAGAACATG
GCCTCATTGATGCTTGGGCTTACATCAGGAAATACTGATCTCTCCAGAACAGTCCCT
CAGCTCGAAAGTAAGGGATTAACACTGAATGTAATGCCTGGATGAACGACACTGTCATAAT
TGATAGTACAGTGGAAAGGACACGTTCTTCTCATCACATGGAACAGTCTGCCCTCCAGTA
TTCTCTGGGATCCAGTGGAAACAATAATGGAAAATTTCACAGTGGATGCAACTTCCAAA
ATGGCCTATCTCAGTATTCCAGGAACCTGCAAAAGTGGGCACTTGGGATACAAATTCAGC
CAAAGCGAACCCAGAAACATTAACATTACAGTAACCTCTCGAGCAGCAAATTCTCTGTG
CTCCAATCACAGTGAATGCTAAATGAATAAGGACGTAAACAGTTCCCCAGCCAATGATT
GTTTACGCAGAAATTCTACAAGGATATGTAACCTGTTCTGGAGCCAATGTGACTGTTCAT
TGAATCACAGAATGGACATACAGAAGTTGGAACTTTGGATAATGGTGCAGGGCTGATT
CTTCAAGAATGATGGAGTCACTCCAGGTATTTCAGCATATAACAGAAAATGGCAGATAT
AGCTTAAAAGTCTGGGCTCATGGAGGAGCAAACACTGCCAGGCTAAAATTACGGCTCCACT
GAATAGAGCCGCTACATACCGGCTGGTAGTGAACGGGAAATTGAAGCAAACCCGCCAA
GACCTGAAATTGATGAGGATACTCAGACCCACCTGGAGGATTTCAGCCGAACAGCATCCGGA
GGTGCATTGGTGGTATCACAAGCTCCAGCCTCCCTGCTGACCAATACCCACCAAGTCA
AATCACAGACCTTGATGCCACAGTTCATGAGGATAAGATTATTCTACATGGACAGCACCAG
GAGATAATTGATGTTGGAAAAGTTCAACGTATATCATAAGAATAAGTGCAGTATTCTT
GATCTAAGAGACAGTTGATGATGCTCTCAAGTAATAACTACTGATCTGTCACCAAAGGA
GCCAACTCCAAGGAAAGCTTGCAATTAAACAGAAAATCTCAGAAGAAAATGCAACCC
ACATATTATTGCCATAAAAGTATAGATAAAAGCAATTGACATCAAAGTATCCAACATT
GCACAACTGACTTGTATTCCCTGATGAAACACTCTGATGACATTGATCTACACCTACTCC
TACTCCTACTCCTACTCTGATAAAAGTCATAATTCTGGAGTTAATTATTCTACGCTGGTAT
TGTCTGTGATTGGGCTGTTGTAATTGTTAACTTATTGTTAAGTACCACTT**TGAACCTA**
ACGAAGAAAAAAATCTCAAGTAGACCTAGAAGAGAGTTTAAAAACAAAACATGTAAGT
AAAGGATATTCTGAATCTAAAATTCACTCCATGTGTGATCATAAAACTCATAAAAATAATT
TTAAGATGTCGGAAAAGGATACTTGATTAATAAAACACTCATGGATATGTAAGAAACTGT
CAAGATTAAAATTAAATAGTTCAATTATTGTTATTGTTAAGGAAATAGTGTGAAAC
AAAGATCCTTTCTACTGATACCTGGTTGTATATTATTGATGCAACAGTTCTGAAAT
GATATTCAAAATTGCAAGAAATTAAAATCATCTATCTGAGTAGTCAAAACACAAGTAAA
GGAGAGCAAAATAAACACATTGGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAA
AAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAAAAGAAAA

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FIGURE 274

MGLFRGFVFLVLCLLHQSNSTFIKLNNNGFEDIVIVIDPSVPEDEKIEQIEDMVTTASTY
LFEATEKRFFFKNVSILIPENWKENPQYKRPKHENKHADIVIVAPPTLPGRDEPYTKQFTEC
GEKGEYIHFTPDLGGKKQNEYGPPGKLFVHEWAHLRWGVFDEYNEDQPFYRAKSKKIEATR
CSAGISGRNRVYKCQGGSCLSRACRIDSTTKLYGKDCQFPDKVQTEKASIMFMQSIDSVVE
FCNEKTHNQEAPSLQNIKCNFRSTWEVISNSEDFKNTIPMVTPPPPPVFSLLKISQRIVCLV
LDKSGSMGGKDRLNRMNQAAKHFLQTVENGSWGMVHFDSTATIVNKLIQIKSSDERNTLM
AGLPTYPLGGTSICSGIKYAFQVIGELHSQLDGSEVLLLTGEDNTASSCIDEVKQSGAIVH
FIALGRAADEAVIEMSKitGGSHFYVSDEAQNNGLIDAFGALTSGNTDLSQKSLQLESKGLT
LNSNAWMNDTVIDSTVGKDTFFLITWNSLPPSISLWDPSGTIMENFTVDATSKMAYLSIPG
TAKVGTWAYNLQAKANPETLTITVTSRAANSSVPPITVNAKMNDVNSFPSPMIVYAEILQG
YVPVLGANVTAFIESQNGHTEVLELLDNGAGADSFKNNDGVYSRYFTAYTENGRYSLKVRAGH
GANTARLKLRLPPLNRAAYIPGWVVNGEIEANPPRPEIDEQTTLTQTTLEDFSRTASGGAFVVSQV
PSLPLPDQYPPSQITDLDATVHEDIKIIILTWTAPGDNFDVGKVQRYIIRISASILDLRDSFDD
ALQVNTTDLSPKEANSKESFAFKPENISEENATHIFIAIKSIDKSNLTSKVSNIAQVTLFIP
QANPDDIDPTPTPTPTPDKSHNSGVNISTLVLSEIGSVVIVNFILSTTI

Signal peptide:

amino acids 1-21

Putative transmembrane domains:

amino acids 284-300, 617-633

Leucine zipper pattern.

amino acids 469-491, 476-498

N-glycosylation site.amino acids 20-24, 75-79, 340-344, 504-508, 542-546, 588-592,
628-632, 811-815, 832-836, 837-841, 852-856, 896-900

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FIGURE 275

CTCCTTAGGTGGAAACCCCTGGGAGTAGAGTACTGACAGCAAAGACCGGGAAAGACCATACGTCCCCG
 GGCAGGGGTGACAACAGGTGTCACTTTTGATCTGTTGCTGGCTGCCCTCCATTCAAGGAAAG
 ACGCCAAGGTATTTGACCCAGAGGAGCAATGATGTAGCCACCTCTAACCTCCCTTGAACC
 CCCAGTTATGCCAGGATTACTAGAGAGTGTCAACTCAACCAGCAAGCGGCTCTCGGCTTAACCT
 GTGGTTGGAGGGAGAGAACCTTGTGGGCTGCGTTCTCTAGCAGTGTCAAGAAGTGACTTGCCTGA
 GGGTGGACCAGAAGAAGGAAGGCTCCCTCTGCTGTGGCTCACATCAGGAAGGCTGTGATGGG
 AATGAAGGTGAAAATGGAGATTCACTGAGTGTGGCTCTGCTGTGGCTCACATCCTTAAAGA
 GTAGAGAAGCTGCTCTGTTGTTAACCTCAAGAGGGCAGAACCTGTTCTAGAAGGAAATGGATG
 CAAGCAGCTCCGGGGGCCAAACGCATGCTCTGTGGCTAGGCCAGGGAAAGCCCTCCGTGGGG
 GCCCGGCTTGTAGGGATGCCACCGGTTCTGGACGCATGGCTGATTCTGA**ATGATGATGGT**CGCC
 GGGGCTGCTGCGTGGATTCCCGGTTGTGGTTTGCTGGTCTCTGCTGTGCTATCTCTGT
 CCTGTACATGTTGGCTGCACCCAAAAGGTGACGAGGAGCAGCTGGACTGCCAGGGCAACAGC
 CCCACGGGAAGGAGGGTACAGGCCGCTCAGGAGTGGAGCAGCAGGGCAACTACGTGA
 GCAGCCTGAAGCGGAGATCGCACAGCTCAAGGAGGAGCTGCAGGGAGAGTGGAGCTCAGGAA
 TGGCAGTACCAAGCCAGCGATGCTGCTGGCTGGACAGGGAGGCCAGAGAGAAAACCCAG
 GCCGACCTCTGGCCTCTGCACTCGCAGGTGGACAAGGCAGAGGTGAATGCTGGCGTCAAGCTGG
 CCACAGAGTATGCACTGCAGTGCCTTGCATAGCTTACTCTACAGAAAGGTGACAGCTGGAGACTGG
 CCTTACCCGCACCCGAGGAGAACGCTGTGAGGAGACAAGCGGGATGAGTTGGTGAAGGCCATT
 GAATCAGCCTTGAGACCCCTGAACAATCTGCAAGAACAGGCCCAATCACCGTCTTACACGGCT
 CTGATTTCATAGAAGGGATCTACCGAACAGAAAGGGACAAGGGACATTGTATGAGCTCACCTCAA
 AGGGGACCACAAACACGAATTCAAACGGCTCATCTATTGACCATTCAGCCCCATCATGAAAGTG
 AAAATGAAAAGCTCAACATGGCAACACGCTTATCAAATGTTATCGTGCCTCTAGCAAAAAGGGTGG
 ACAAGTCCGGCAGTTCATGCAGAATTTCAGGGAGATGTCATTGAGCAGGATGGGAGAGTCCACATCT
 CACTGTTTACTTGGAAAGAAGAAAATTAATGAAGTCAAAGAACATTTCTGGGGAAAGGGACTTG
 GCTGCCAACCTCAGGAACATTACCTCATCCAGCTGAATGGAGAATTTCCTGGGGAAAGGGACTTG
 ATGTTGGAGCCGTTCTGGAAAGGAAGCAACGTCCTCTCTGTGATGTGGACATCTACTT
 CACATCTGAATTCCCTAATACGTGAGGCTGAATACACAGCCAGGGAAAGAAGGTATTTATCCAGTT
 CTTTCAGTCAGTACAATCCTGGCATAATATACGGCCACCATGATGCACTCCCTCCCTGGAACAGC
 AGCTGGTCATAAAGAAGGAAACTGGATTGGAGAGACTTGGATTGGGATGACGTGTCAGTATCG
 GTCAAGACTTCATCAATATAGGTGGTTGATCTGGACATCAAAGGCTGGGGCGAGAGGATGTGCAAC
 CTTATCGCAAGTATCTCCACAGCAACCTCATGTTGACGGCTGTGGCAGGACTCTCCACC
 TCTGGCATGAGAAGCGCTGCATGGACGAGCTGACCCCCGAGCAGTACAAGATGTGCATGCAGTCCAA
 GGCATGAACGAGGCATCCCACGCCAGCTGGCATGCTGGTGTCAAGGAGATAAGGGCTCAC
 CTCGCCAACAGAACAGAACAGAACAGAACAGAACAGAACAGAACAGAACAGAACAGAACAG
 CACCTTTCTTCCTTGCATTGCAATTACTGAAAGTGGCTGCAACAGAACAGAACAGAACAG
 AACAAAAGAACATGGACTGATGGGTGAGAGATGAGAACAGCCTCCGATTCTCTGTTGGCTTTAC
 AACAGAAATCAAATCTCCGTTGCTGCAAAAGTAACCCAGTTGCACCCCTGTGAAGTGTCTGACA
 AAGGCAGAATGCTGTGAGATTATAAGCCTAATGGTGTGGAGGTTTGATGGTGTAACTACACT
 GAGACCTGTTGGTTGCTGAGTTAGTCTGCTTAAATATTGATGTTAAAGAGCAGTTGGTAAAGAAC
 TAGCATGAAAGGCATATTCTCTCATGATGAGAACAGCTGATGAGGCTATCAGCAGGGCTCTAGTTCTAGG
 AATGCTAAATATCAGAAGGCAGGGAGAGGAGATAGGCTTATTATGATACTAGTGGACTACATTAGTA
 AAATAAAATGGACCAGAAAAGAAAAGAACATAAATATCGTGTCAATTCTCCCAAGGATTAACCA
 AAAATAATGCTTATCTTTGGTTGCTTTAACCTGCTCCCTTTCTTTTATTTAAAT
 GCACATTCTTCTCCCTGAGTTAGTCTGCTTAAATACCAACTTGCACGCTTACAAGAGA
 GCACAAGTGGCCTACATTCTTATTTAAAGAACGACTTGGAGATGCAATTATGAGAACACTTCA
 GTTCAAAGCATCAAATTGATGCCATTACCAAGGACATGCCAAATGCTGATTCTGTCAGGCACGTGAAT
 GTCAAGGATTGAGACATAGGGAGGAATGGTTGACTAATACAGACGTACAGATACTTCTCTGAA
 GAGTATTTGAGAGGAGCAACTGAAACACTGGAGGAAAAGAAAATGACACTTCTGCTTACAGAA
 AAGGAAACTCATTGAGACTGGTGTACCTAAAGTCAGAACACCACATTCTCTCTCA
 GAAGTAGGGAGCGCTTCTTACCTGTTAAATAACCAAGTATAACCGTGTGAACCAAAACATCT
 TTCAAAACAGGGTGTCTCTCTGGCTTCTGCTTCAAGAAGAAATGGAGAAAATATATAT
 ATATATATATATTGATGAAAGATCAATCCATCTGCCAGAATCTAGTGGGATGGAAGTTTGCTACAT
 GTTATCCACCCAGGCCAGGTGGAGTAACCTGAAATTATTTAAATTAGCAGTCTACTCAATCA
 CCAAGATGCTCTGAAAATTGCAATTCTTATTACCAATTCAAACTATTGTTAAATAACAGTAA
 ACATAGAGTGGTTCTTCATTGATGAAAATTATTAGCCAGCACCAGATGCAATTATCT
 CTTGAGTCCCTGCTTGTGTTGCTCACAGTAAACTCAATTGTTAAAAGCTCAAGAACATTCAAGC
 TGTGGTGTGTTAAATAATGCAATTGATTTGACTGGTAGTTATGAAATTAAATTAAACAC
 AGGCCATGAATGGAAGGTGGTATTGCACAGCTAATAAAATATGATTGTGGATATGAA

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FIGURE 276

MMMVRRGLLAWISRVVVLLVLLCCAISVLYMLACTPKGDEEQLALPRANSPTGKEGYQAVLQ
EWEEQHRNYVSSLKRQIAQLKEELQERSEQLRNGQYQASDAAGLGLDRSPPEKTQADLLAFL
HSQVDKAEVNAGVKLATEYAAVPFDSFTLQKVYQLETGLTRHPEEKPVRKDKRDELVEAIES
ALETLNNPAENSPNHRPYTASDFIEGIYRTERDKGTLYELTFKGDHKHEFKRLILFRPFSP
MKVKNEKLNMANTLINVIVPLAKRVDKFRQFMQNFR
EMCIEQDGRVHLTVVYFGKEEINEVK
GILENTSKAANFRNFTFIQLNGEFSRGKGLDVGARFWKGSNVLLFFCDVDIYFTSEFLNTCR
LNTQPGKKVFPVLFQSQYNPGIIYGHDAVPPLEQQLVIKKETGFWRDFGFGMT
CQYRSDFI
NIGGFDL
DIKGWGGEDVHLYRKYLHSNLIVVTPV
RGLFHLWHEKRCMDELTPEQYK
MCMQS
KAMNEASHGQLGMLVFRHEIEAHLRKQKQTSSKKT

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FIGURE 277

GAAGAA**T**GTGGCTGCTTTCTGGTACTGCCATTATGCTGAACCTGTCAACC
AGGTGCAGAAAATGCTTTAAAGTGAGACTTAGTATCAGAACAGCTCTGGGAGATAAGCAT
ATGCCTGGATACCAATGAAGAATACCTCTCAAAGCGATGGTAGCTTCTCCATGAGAAAA
GTTCCCAACAGAGAACGAAACAGAAATTCCCAGTCCTACTTGCAATGTAACCCAGAGGGT
ATCATTCTGGTTGTGGTTACAGACCCCTTCAAAAATCACACCCCTCCTGCTGTTGAGGTGC
AATCAGCCATAAGAATGAA**C**AGAACCGGATCAACAAATGCCTTCTTCTAAATGACCAAAC
CTGGAATTTTAAAATCCCTCCACACTTGCAACCACCATGGACCCATCTGTGCCCATCTG
GATTATTATATTGGTGTGATATTGCATCATCATAGTTGCAATTGCACTACTGATT
CAGGGATCTGGCAACGTAGAAGAAAGAACAAAGAACCATCTGAAGTGGATGACGCTGAAGAT
AAAGTGTGAAAACATGATCACAATTGAAAATGGCATCCCTCTGATCCCCTGGACATGAAGGG
GGGCATATTAATGATGCCTCA**TG**A**C**AGAGGATGAGAGGCTCACCCCTCTGAAGGGCTGT
TGTTCTGCTCCTCAAGAAATTAAACATTGTTCTGTGACTGCTGAGCATCCTGAAATA
CCAAGAGCAGATCATATATTGTTCAACCATTCTCTTGTAA**T**TTGAATGTGCT
TGAAAGTAAAAGCAATCAATTACCCACCAACACCCTGAAATCATAAGCTATTACGAC
TCAAAATATTCTAAAATATTGTTCTGACAGTATAGTGTATAAATGTGGTATGTGGTATTG
TAGTTATTGATTAAAGCATTGTTAGAAATAAGATCAGGCATATGTATATATTTCACACTTC
AAAGACCTAAGGAAAATAAATTCCAGTGGAGAATACATATAATATGGTAGAAATCAT
TGAAAATGGATCCTTTGACGATCACTTATATCACTCTGTATATGACTAAGTAAACAAAAG
TGAGAAGTAATTATTGTAATGGATGGATAAAATGGAATTACTCATATACAGGGTGGATT
TTATCCTGTTATCACACCAACAGTTGATTATATATTCTGAATATCAGCCCTAATAGGAC
AATTCTATTGTTGACCATTCTACAATTGAAAAGTCCAATCTGTGCTAACTTAATAAAG
TAATAATCATCTTTTAAAAA

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FIGURE 278

MLWLLFFLVTIAHAEIQCQGAENAFKVRLSIRTALGDKAYAWDTNEEYLFKAMVAFSMRKVP
NCREATEISHVLLCNVTQRVSFWVTDPSKNHTLPAVEVQSAIRMNKNRINNAFFLNDQTLE
FLKIPSTIAPPMDPSVPIWIIIFGVIFCIIIVAIALLILSGIWQRRRKNEPSEVDDAEDKC
ENMITIENGIPSDPLDMKGGILMMPS

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FIGURE 279

AACTCAAACCTCTCTGGGAAAACGCGGTGCTGCTCCTCCGGAGTGGCCTTGGCAGG
GTGTTGGAGCCCTCGGTCTGCCCGTCCGGTCTCTGGGGCCAAGGCTGGTTCCCTATGT
ATGGCAAGAGCTCTACTCGTGCAGGTGCTTCTCCTGGCATAACAGCTCACAGCTTTGG
CCTATAGCAGCTGTGAAATTATACCTCCGGGTGCTGGAGGCTGTTAATGGGACAGATGC
TCGGTTAAAATGCACTTCTCCAGCTTGCCCCGTGATGCTCTAACAGTGACCTGGA
ATTTCGTCCCTCTAGACGGGGGACCTGAGCAGTTGTATTCTACTACACATAGATCCCTC
CAACCCATGAGTGGCGGTTAAGGACCGGGTGTCTGGATGGGAATCCTGAGCGGTACGA
TGCCTCCATCCTCTGGAAACTGCAGTTGACGACAATGGGACATAACACCTGCCAGGTGA
AGAACCCACCTGATGTTGATGGGGTGTAGGGGAGATCCGGCTCAGCGTCGTGCACACTGTA
CGCTTCTCTGAGATCCACTTCCTGGCTCTGGCATTGGCTCTGCCTGTGCACTGATGATCAT
AATAGTAATTGTTAGTGGCCTCTCCAGCATTACCGAAAAAGCGATGGGCCAAAGAGCTC
ATAAAGTGGTGGAGATAAAATCAAAGAAGAGGAAAGGCTCAACCAAGAGAAAAAGGTCTCT
GTTTATTTAGAAGACACAGACTAACAATTAGATGGAAGCTGAGATGATTCCAAGAACAA
GAACCCTAGTATTCTGAAGTTAATGAAACTTTCTTGCTTCCAGTTGTGACCCGT
TTTCCAACCAGTTCTGCAGCATATTAGATTCTAGACAAGCAACACCCCTCTGGAGCCAGCAC
AGTGCCTCCATATCACCAGTCATACACAGCCTCATTATTAAGGTCTTATTTATTCAGA
GTGTAATTTTCAAGTGCCTAGGTTATAAAACAAGAAGCTACATTTGCCCTAA
GACACTACTACAGTGTATGACTGTATACACATATATTGGTATCAAAGGGATAAAAGCC
AATTTGTCTGTTACATTCTTACGTATTCTTAGCAGCACTCTGCTACTAAAGTTA
ATGTGTTACTCTTCCCTCCACATTCTCAATTAAAGGTGAGCTAAGCCTCCTGGTG
TTCTGATTAACAGTAAATCTAAACTGTTAAATGACATTATTTATTTATGTCTC
TCCTTAACATGAGACACATCTGTTACTGAATTCTTCAATATTCCAGGTGATAGATT
TTTGTGCG

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FIGURE 280

MYGKSSTRAVLLLGIQLTALWPIAAVEIYTSRVLEAVNGTDARLKCTFSSFAPVGDALTWT
WNFRPLDGGPEQFVFYYHIDPFQPMGRFKDRVSDGNPERYDASILLWKLQFDDNGTYTCQ
VKNPPDVGVIGEIRLSVVHTVRFSEIHFLALAIGSACALMIIIVVVVLFQHYRKKRWAER
AHKVVIEIKSKEEERLNQEKKVSVYLEDTD

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FIGURE 281

GCATTTGTCTGTGCTCCCTGATCTCAGGTACCCACCATGAAGTTCTTAGCAGTCCTGGT
ACTCTGGGAGTTCCATCTTCTGGTCTCTGCCAGAACAGCTGCTCCAGCTG
ACACGTATCCAGCTACTGGTCCTGCTGATGATGAAGCCCTGATGCTGAAACCAGCTGCTGCTG
GCAACCACTGCGACCACTGCTGCTCCTACCACTGCAACCACCGCTGCTTCTACCACTGCTCG
TAAAGACATTCCAGTTACCCAAATGGGTTGGGATCTCCGAATGGTAGAGTGTGTCCCT
GAGATGGAATCAGCTTGAGTCTCTGCAATTGGTCACAACATTGCTTCCTGTGATTTC
ATCCAACTAACCTACCTGCCTACGATATCCCCTTATCTCTAATCAGTTATTTCTTCAA
ATAAAAAAATAACTATGAGCAACATAAAAAAAAAAAAAA

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FIGURE 282

MKFLAVLVLLGVSIFLVSAQNPTTAAPADTYPATGPADDEAPDAETTAATTATTAAAPTTAT
TAASTTARKDIPVLPKWVGDLPNGRVCP

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FIGURE 283

GGACTCTGAAGGTCCCAAGCAGCTGCTGAGGCCCAAGGAAGTGGTCCAACCTTGGACCC
CTAGGGGTCTGGATTTGCTGGTTAACAGATAACCTGAGGGCAGGACCCATAGGGGAATGC
TACCTCCTGCCCTTCCACCTGCCCTGGTGTACGGTGGCCTGGTCCCTCCTGCCGAGAGA
GTGTCCTGGTCAGGGACGCAGAGGACGCTCACAGACTCCAGCCTTGTTACCGAGAGGAC
ACTTGGCAAGGTCCAGCGATGGTCCGGAGTCCACACACAGACTGGCGCAGGGCAGGAGGG
GACAGTTCTGTTGTGCTGGTGGACAGTAAGAGGGTCTGGCCAGTCCAGGGTGGGGCG
GCAAACCTCCATAAAGAACCAAGAGGGTCTGGGCCACAGAGTCATCTGCCAGCTCCT
CTGCTGCCAGTGGAGTGGCACGAGGTGGGCTTGCCAGAAAACCACAGGCTGG
ATTGCTGCCAGTGGAGTGGCACGAGGTGGGCTTGCCAGAAAACCACAGGCTGG
CCCCAAAGAGCTTCATTGTATCTATTGATTTTACACATTAGCAATTAAACTGAGAAAT
GGGCCGGCACGGTGGCTCACGCCGTAAATCCCAGCACTTGGGAGGCCAGGGGGTGGAT
CACCTGAGATCAGGAGTTCAAGACCAGCCTGGCCAACATGGTGAAACCTTGTCTACTAAAAA
TACAAAAAAATTAGCCAGGCACAGTGGTGTGCACTGGTAGTCCAGTTACTCGGGAGGCTGAG
GCAGGAAAATCGCTTGAACCCAGGAGGCGGACGTTGCGGTGAGCCAGATCGCGCCGCTGAT
TCCAGCCTGGCGACAAGAGTGGACTCCATCTCACACA

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FIGURE 284

MLPPALPPALVFTVAWSLLAERVSVRDAEDAHRLQPFVTERTLGKVQRWSGVHTQTGGRAG
GGQFCCAWLDSKRVLASPGWGAANSIKNQRVWAPATESSAQLLCCWPVGVARGGALCQ

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FIGURE 285

GTCATGCCAGTGCCTGCTCTGTGCCTGCTCTGGGCCCTGGCAATGGTACCCGGCTGCCTCA
GCGGCCCCATGGCGGCCAGAACTGGCACAGCATGAGGAGCTGACCCCTGCTTTCCATGG
GACCCTGCAGCTGGGCCAGGCCCTCAACGGTGTGTACAGGACCAACGGAGGGACGGCTGACAA
AGGCCAGGAACAGCCTGGGTCTCTATGGCCGCACAATAGAACTCCTGGGGCAGGAGGTCAAGC
CGGGGCCGGGATGCAGCCCAGGAACCTCAGGGCAAGCCTGTTGGAGACTCAGATGGAGGAGGA
TATTCTGCAGCTGCAGGCAGAGGCCACAGCTGAGGTGCTGGGGGAGGTGGCCAGGCACAGA
AGGTGCTACGGACAGCGTGCAGCGCTAGAAGTCCAGCTGAGGAGCGCCTGGCTGGCCCT
GCCTACCGAGAATTGAGGTCTTAAAGGCTCACGCTGACAAGCAGGCCACATCCTATGGGC
CCTCACAGGCCACGTGCAGCGCAGAGGCCGGAGATGGTGGCACAGCAGCATGGCTGCGAC
AGATCCAGGAGAGACTCCACACAGCGGCCTCCAGCTTGAATCTGCCTGGATGGAACGTGAG
GACCAATCATGCTGCAAGGAACACTTCCACGCCCGTGAAGGCCCTGTGCAGGGAGGAGCTG
CCTGTTCACTGGGATCAGCCAGGGCGCCGGGCCCCACTTCTGAGCACAGCAGAGACAGAC
GCAGGGGGGACAAAGGCAGAGGATGTAGCCCCATTGGGGAGGGGTGGAGGAAGGACATGTA
CCCTTCATGCCTACACACCCCTCATTAAAGCAGAGTCGTGGCATTCAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAA

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FIGURE 286

MPVPALCLLWALAMVTRPASAAPMGGPELAQHEELLLFHGTLQLQALNGVYRTTEGRLTK
ARNSLGLYGRTIELLGQEVSGRDAAQELRASLLETQMEEDILQLQAEATAEVLGEVAQAQK
VLRDSVQRLEVQLRSAWLGPAYREFEVKAHADKQSHILWALTGHVQRQRREMVAQQHRLRQ
IQERLHTAALPA

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FIGURE 287

GGCAACATGGCTCAGCAGGCTTGC~~CCC~~CAGAGCCATGGCAAAGAATGGACTTGTAATTGCAT
CCTGGT~~GAT~~CAC~~CTT~~ACTCCTGGACCAGACCAGCCACACATCCAGATTAAAGCCAGGA
AGCACAGCAAACGTCGAGTGAGAGACAAGGATGGAGATCTGAAGACTCAAATTGAAAGCT
TGGACAGAAGTCAATGC~~CTT~~GAAGGAAATTCAAGCC~~CTG~~CAGACAGTCTGTCTCGAGGCAC
TAAAGTT~~CACA~~AGAAATGCTAC~~CTT~~GCTTCAGAAGGTTGAAGCATTCCATGAGGCCAATG
AAGACTGCATTCCAAAGGAGGAATC~~CTG~~TTATCCCAGGAACTCCGACGAAATCAACGCC
CTCCAAGACTATGGTAAAGGAGGACGCTGCCAGGTGTCAATGACTTTGGCTGGGATCAATGA
CATGGTCACGGAAAGGCAAGTTGTTGACGTCAACGGAATCGCTATC~~CC~~CTC~~CT~~CAACTGGG
ACCGTGCACAGC~~TA~~ACGGTGGCAAGCGAGAAAACTGTGT~~CT~~GT~~CT~~CC~~TA~~ACTCAGCTCAG
GGCAAGTGGAGT~~GAT~~GAGGC~~CTG~~CAGCAGCAAGAGATACATATCGAGTT~~AC~~CCATCCC
TAAATAGGT~~CTT~~CTCAATGTG~~CT~~CC~~TA~~AGCAAGATT~~CAT~~CATAACTTATAGGTT~~CAT~~GA
TCTCTAAGATCAAGTAAAAATC~~ATA~~TTT~~TACTT~~TATTAAAAAAATGCAACACAAGATCAAT
GTCCATAGCAATATGATAGC~~AT~~CAG~~CC~~ATTTGCTAACAC~~AC~~ATT~~CTT~~GGGAT~~TTT~~GC~~CC~~
TC~~CT~~GGGGTATAGGGATCAGAAATATTGATCC~~AT~~GTGCACG~~CAG~~ATAAAATGG~~CT~~CTG~~CT~~
AAACAGACTAAAAAT~~CTT~~CT~~CT~~AGT~~CTT~~CT~~CA~~TTGTACAAACCCAG~~TTT~~GT~~TTT~~CAA
AAATCACAGTAGCAATGCAACTC~~AT~~CACTTAAGAAAGCAAGCTTAGG~~GT~~AC~~CT~~GAAAGATT
TTCC~~CT~~GGAAAGTTAG~~GT~~T~~GT~~TTGACTAACAAAAT~~CC~~CTAC~~AT~~CAGAGACT~~CT~~AG~~GT~~
GCTATATAATCCAAAAACT~~TTT~~CAGC~~CT~~GT~~TT~~GCT~~ATT~~CTG~~CCC~~ATG~~CT~~GG~~CA~~ATAATACC
TTGTCAG~~CC~~ATTAC~~CC~~TTATT~~TT~~GAATTG~~CT~~CC~~AT~~CTC~~CT~~GG~~GG~~ACT~~GT~~T~~AT~~CT~~GT~~CT
GCCATATCAGAACACAAACCCCTGAAGAGGTT~~CT~~GATTGATT~~TTT~~TTT~~TTT~~CT~~TC~~ATGCC
TACCC~~TTT~~GGAAAGTTCCAG~~CC~~GAATTGAAATGAAATGACAGGT~~GT~~T~~AT~~TTGAT
CAATTTC~~AT~~CC~~AC~~ATT~~G~~CATTAC~~AC~~CT~~TA~~ACT~~AA~~ATGG~~TA~~AC~~CC~~CT~~AA~~AGG~~CA~~T~~AT~~
CAAAGAAGCAGATT~~G~~CAT~~G~~ATAAACG~~GA~~AT~~G~~AAGAAAAGAAC~~CT~~AC~~AT~~TT~~TT~~G~~CT~~TT
AGC~~AT~~C~~CT~~T~~ACT~~CT~~CAC~~TTT~~TAT~~GAGATTGAGAG~~GT~~GGACT~~TAC~~ATT~~CC~~TTT~~TAC~~ATT
TC~~GT~~T~~AT~~TT~~TAT~~TTT~~TAG~~CC~~AT~~C~~ATT~~AT~~AT~~G~~TT~~AAG~~GT~~T~~ATT~~ATGG~~CA~~AC~~CA~~AT~~CT~~
TGGAAAGCTGAAAACT~~GA~~ATT~~AA~~AGAATGCT~~AT~~CT~~GG~~AAATGC~~AT~~AC~~GT~~CT~~GT~~GC~~AA~~TT
TTT~~TAT~~CT~~GC~~CT~~AG~~T~~G~~CT~~ATT~~CT~~G~~CT~~TT~~TAACTAGATT~~G~~T~~AC~~AAATAAACTTC~~ATT~~G~~CT~~
TAATAT~~CA~~AAATTAACAAAGTT~~TAG~~ACT~~TG~~GAGGGAAATGGCT~~TTT~~TAGAAG~~CA~~AAACAAAT
AAATAT~~ATT~~T~~GT~~T~~CT~~CAAATAAATAG~~GT~~TTAAACATT~~G~~AATGT~~TTT~~GT~~GA~~AC~~AA~~AT~~AT~~
CCC~~ACT~~TTG~~CA~~AAACTTT~~AA~~ACT~~AC~~AC~~AT~~G~~CT~~GG~~AA~~TT~~AA~~AG~~TTT~~AG~~CT~~GT~~TTT~~C~~ATT~~G~~CT~~CA
ATAATAAAGCCT~~GA~~ATT~~CT~~G~~AT~~CAATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 288

MAQQACPRAMAKNGLVICILVITLLLDDQTSHTSRLKARKHSKRRVRDKDGDLKTQIEKLWT
EVNALKEIQALQTVCLRGTKVHKKCYLASEGLKHFHEANEDCISKGGILVIPRNSDEINALQ
DYGKRSLPGVNDFWLGINDMVTEGFVDVNGIAISFLNWDRAQPNGGKRENCVLFQSQAQGK
WSDEACRSSKRYICEFTIPK

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FIGURE 289

GCAGGGACCGGGTATAAGAAGCCTCGTGGCCTTGCCCCGGCAGCCGCAGGTTCCCCGCGC
CCCGAGCCCCCGCGCC **ATGA**AGCTCGCCGCCCTCCTGGGGCTCTGCGTGGCCCTGTCTGCA
GCTCCGCTGCTGTTCTTAGTGGCTCGGCCAAGCCTGTGGCCAGCCTGCGCTGCGCTG
GAGTCGGCGGCGGAGGCCGGGGCCGGGACCCCTGGCCAACCCCCCTCGGCACCCCTAACCCGCT
GAAGCTCCTGCTGAGCAGCCTGGGCATCCCCGTGAACCACCTCATAGAGGGCTCCAGAAGT
GTGTGGCTGAGCTGGTCCCCAGGCCGTGGGGCCGTGAAGGCCCTGAAGGCCCTGCTGGGG
GCCCTGACAGTGTGGCT**TGA**GCCGAGACTGGAGCATCTACACCTGAGGACAAGACGCTGCC
CACCCGCGAGGGCTGAAAACCCCGCCGCGGGGAGGACCGTCCATCCCCCTCCCCCGGCCCT
CTCAATAAACGTGGTTAAGAGCAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAA

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FIGURE 290

MKLAALLGLCVALSCSSAAAFLVGSAKPVAQPVALESAAEAGAGTLANPLGTLNPLKLLLS
SLGIPVNHLIEGSQKCVaelGPQAVGAVKALKALLGALTIVFG

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FIGURE 291

TGAAGGACTTTCCAGGACCCAGGCCACACACTGGAACTTGCAGCTGAAGGGAGGCAC
CCTTGGCCTCCGCAGCCGATCACATGAAGGTGGTGCCAAGTCTCCTGCTCTCCGCTCTCG
GCACAGGTGTGGCTGGTACCCGGCTGGCCCCAGTCCTCAGTCGCCAGAGACCCAGCCCC
TCAGAACCAAGACCAGCAGGGTAGTGCAGGCTCCAGGGAGGAAGAGGAAGATGAGCAGGAGG
CCAGCGAGGAGAAGGCCGGTGGAGGAAGAGAAAGCCTGGCTGATGCCAGCAGCAGCAGCTT
GCCAAGGAGACTTCAAACCTCGGATTCAAGCCTGCTGCAGAAAGATCTCCATGAGGCACGATGG
CAACATGGTCTTCTCTCCATTGGCATGTCCTGGCCATGACAGGGCTTGATGCTGGGGCCA
CAGGGCCACTGAAACCCAGATCAAGAGAGGGCTCCACTTGAGGCCCTGAAGCCCACCAAG
CCCGGGCTCTGCCTTCCCTTTAAGGGACTCAAGAGAGACCTCTCCCGAACCTGGAAC
GGGCCTCTCACAGGGAGTTTGCTTCATCCACAAGGATTGATGTCAAAGAGACTTTCT
TCAATTATCCAAGAGGTATTTGATACAGAGTGCCTGCTATGAATTTCGCAATGCCTCA
CAGGCCAAAGGCTCATGAATCATTACATTAACAAAGAGACTCGGGGAAAATTCCCAAAC
GTTGATGAGATTAATCCTGAAACCAAATTAAATTCTTGTGGATTACATCTTGTCAAAGGGA
AATGGTTGACCCCATTGACCCCTGTCTCACCGAAGTCGACACTTCCACCTGGACAAGTAC
AAGACCATTAAAGGTGCCATGATGTACGGTGCAGGCAAGTTGCCTCACCTTGACAAGAA
TTTCGTTGTCATGTCCTCAAACCTGCCCTACCAAGGAAATGCCACCATGCTGGGGCCTCA
TGGAGAAAATGGGTGACCACCTGCCCTGAGACTACCTGACCACAGACTTGGGAGACA
TGGCTCAGAAACATGAAAACAGAAACATGGAAGTTCTTCCGAAGTTCAAGCTAGATCA
GAAGTATGAGATGCATGAGCTGCTTAGGCAGATGGGAATCAGAAGAATCTCTCACCCCTTG
CTGACCTTAGTGAACCTCAGCTACTGGAAGAAATCTCAAAGTATCCAGGGTTTACGAAGA
ACAGTGATTGAGTTGATGAAAGGGGACTGAGGCAGTGGCAGGAATCTGTCAGAAATTAC
TGCTTATTCCATGCCCTGTCATCAAAGTGGACCAGGCCATTTCATTCATGATCTATGAAG
AAACCTCTGGAATGCTCTGTTCTGGCAGGGTGGTGAATCCGACTCTCCTATAAATTCA
ACATGCATAAGCACTTCGTGCTGAGTAGATGCTGAATCTGAGGTATCAAACACACAGGA
TACCAAGCAATGGATGGCAGGGGAGAGTGTCCCTTTGTTCTTAACTAGTTAGGGTGTCTC
AAATAAAATACAGTAGTCCCCACTTATCTGAGGGGATACATTCAAAGACCCAGCAGATGC
CTGAAACGGTGGACAGTGCCTGAAACCTTATATATTTTCTACACATACACCTATGAT
AAAGTTAATTATAAATTAGGCACAGTAAGAGATAACAATAACAACATTAAAGTAAAAA
TGAGTTACTGAAACGCAAGCAGTCAATACCAAAACAGTCAGTCAACTGATTATAGAGAAGGCTA
CTAAGTGACTCATGGCGAGGAGCATAGACAGTGTGGAGACATTGGCAAGGGGAGAATTCA
CATCCTGGGTGGACAGAGCAGGACGATGCAAGATTCCACTACTCAGAATGGCATGC
TGCTTAAGACTTTAGATTGTTATTTCTGGAATTTCATTAATGTTTGACCATGGT
TGACCATGGTTAAGTGGACTGAGACTGCAGAAAGCAAAACCATGGATAAGGGAGGACTACTACAAAA
GCATTAATGATACATATTTAAAAAAAAAAAAAA

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FIGURE 292

MKVVPSLLL SVLLAQVWLVPGLAPSPQSPETPAPQNQTSRVVQAPREEEEDEQEASEEKAGE
EEKAWLMASRQQLAKETS NFGFSLLRKISM RHDGNMVFSPFGMSLAMTGLMLGATGPTETQI
KRGLHLQALKPTKPGLLPSLFKGLRETLSRNLELGLSQGSFAFIHKDFDVKETFFNLSKRYF
DTECVPMNFRNASQAKR LMNHYINKETRGKIPKLFDEINPETKLILVDYILFKGKWLTPFDP
VFTEVDTFHLDKYKTIKVPM MYGAGKFASTFDKNFRCHVLKL PYQGNATMLVVLMEKMGDHL
ALEDYLT TDLVETWLRNMKTRNMEVFFPKFKLDQKYEMHELLRQMGIRRI FSPFADL SELSA
TGRNLQVSRVLRRTVIEVDERGTEAVAGILSEITAYSMPPVIKVDRPFHFMIYEETSGMLLF
LGRVVNPTLL

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FIGURE 293

CTGGGATCAGCCACTGCAGCTCCCTGAGCACTCTCTACAGAGACGCAGGACCCAGACATGAG
GAGGCTCCTCCTGGTACCCAGCCTGGTGGTTGTGCTGTGGAGGCAGGTGCAGTCCCAG
CACCCAAAGGTCCCTATCAAGATGCAAGTCAAACACTGGCCCTCAGAGCAGGACCCAGAGAAG
GCCTGGGGCGCCCGTGTGGTGGAGCCTCCGGAGAAGGACGACCAGCTGGTGGTGTGTTCCC
TGTCCAGAAGCCGAAACTCTTGACCACCGAGGAGAAGCCACGAGGTCAAGGCAGGGCAGGGGCC
TCCTTCCAGGCACCAAGGCCTGGATGGAGACCGAGGACACCCTGGCCGTGTCCCTGAGTCCC
GAGCCCGACCATGACAGCCTGTACCACCCCTCCGCCTGAGGAGGACCAGGGCGAGGAGAGGCC
CCGGTTGTGGGTGATGCCAAATCACCAGGTGCTCCTGGACCGGAGGAAGACCAAGACCACA
TCTACCACCCCCAGTAGGGCTCCAGGGCCATCACTGCCCGCCCTGTCCAAGGCCAGG
CTGTTGGACTGGACCCCTCCCTACCCCTGCCAGCTAGACAAATAACCCAGCAGGCAA
AAAAAAAAAAAAAAA

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FIGURE 294

MRRLLLVTSLVVVLLWEAGAVPAPKVKPIKMQVKHWPSEQDPEKAWGARVVEPPEKDDQLVVL
FPVQKPKLLTTEEKPRGQGRGPILPGTKAWMETEDTLGRVLSPEPDHDSLYHPPPEEDQGEE
RPRLWVMPNQVLLGPEEDQDHLYHPQ

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FIGURE 295

AGAAAGCTGCACTCTGTTGAGCTCCAGGGCGCAGTGGAGGGAGGGAGTGAAGGAGCTCTCTG
TACCCAAGGAAAGTGCAGCTGAGACTCAGACAAGATTACAATGAACCAACTCAGCTTCTGC
TGTTCATAGCGACCACCAGAGGATGGAGTACAGATGAGGCTAATACTTAAGGAA
TGGACCTGTTCTCGTCTCCATCTGCCAGAAGCTGCAAGGAAATCAAAGACGAATGTCC
TAGTGCATTGATGGCCTGTATTTCTCCGCACTGAGAATGGTGTATCTACCAAGACCTTCT
GTGACATGACCTCTGGGGTGGCGTGGACCCCTGGTGGCCAGCGTGCATGAGAATGACATG
CGTGGGAAGTGCACGGTGGCGATCGCTGGTCCAGTCAGCAGGGCAGCAAAGCAGACTACCC
AGAGGGGACGGCAACTGGCCAACATACAACACCTTGGATCTGCAGAGGCAGGCCACGAGCG
ATGACTACAAGAACCTGGCTACTACGACATCCAGGCCAAGGACCTGGCATCTGGCACGTG
CCCAATAAGTCCCCCATGCAGCACTGGAGAACAGCTCCCTGCTGAGGTACCGCACGGACAC
TGGCTTCCTCCAGACACTGGGACATAATCTGTTGGCATCTACCAGAAATATCCAGTGAAT
ATGGAGAAGGAAAGTGTGGACTGACAACGGCCCGGTGATCCCTGTGGTCTATGATTGGC
GACGCCAGAAAACAGCATCTTATTACTCACCTATGCCAGCGGGATTCACTGCAGGGATT
TGTTCAAGTTCAAGGTATTAATAACGAGAGAGCAGCCAACGCCCTGTGTGCTGGAATGAGGG
TCACCGGATGTAACACTGAGCATCACTGCATTGGTGGAGGAGGATACTTCCAGAGGCCAGT
CCCCAGCAGTGTGGAGATTTCTGGTTTGATTGGAGTGGATATGGAACTCATGTTGGTTA
CAGCAGCAGCCGTGAGATAACTGAGGCAGCTGTGCTTCTATTCTATCGTTGAGAGTTGTG
GGAGGGAACCCAGACCTCTCCCTCCAACCATGAGATCCAAAGGATGGAGAACAAACTACCA
GTAGCTAGAATGTTAATGGCAGAAGAGAAAACAATAATCATATTGACTCAAGAAAAAA

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FIGURE 296

MNQLSFLLFLIATTRGWSTDEANTYFKEWTCSSSPSLPRSCKEIKDECPSAFDGLYFLRTEN
GVIYQTFCDMTSGGGWTLVASVHENDMRGKCTVGDRSSQQGSKADYPEGDGNWANYNTFG
SAEAATSDDYKNPGYYDIQAKDLGIWHVPNKSPMQHWRNSSLRYRTDTGFLQTLGHNLFGI
YQKYPVKYGEGKCWTDNGPVIHVYDFGDAQKTASYSPYQREFTAGFVQFRVFNNERAAN
ALCAGMRVTGCNTEHHCIGGGGYFPEASPQQCGDFSGFDWSGYGTHVGYSSREITEAAVLL
FYR

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FIGURE 297

GC GGAGCCGGCGCCGGCTGCGCAGAGGAGCCGCTCTGCCGCCACCTCGGCTGGAGCC
CACGAGGCTGCCGCATCCTGCCCTCGAACAAATGGGACTCGCGCGAGGTGCTTGGCG
CGCTGCTCCTGGGGACGCTGCAGGTGCTAGCGCTGGGGCCGCCCAGAACAGCGCAGCC
ATGGCGGCATCTGCAAACATAGAGAATTCTGGGCTTCCACACAACACTCCAGTGCTAACTCAAC
AGAGACTCTCAAACATGTGCCTCTGACCATAAAATGAAACTTCAAACAGTACTGTGAAAC
CACCAACTTCAGTTGCCTCAGACTCCAGTAATAACACGGTACCCACCAGAACCTACAGCG
GCATCTAATAACAACACACCAGGGATGGTCTCAACAAATATGACTTCTACCACCTAAAGTC
TACACCCAAAACAACAAGTGTTCACAGAACACATCTCAGATATCAACATCCACAATGACCG
TAACCCACAATAGTTCAAGTGACATCTGCTGCTTCATCAGTAACAATCACAACACTATGCAT
TCTGAAGCAAAGAAAGGATCAAAATTGATACTGGGAGCTTGTGGTGGTATTGTATTAAC
GCTGGGAGTTTATCTATTCTTACATTGGATGCAAAATGTATTACTCAAGAAGAGGCATTC
GGTATCGAACCATAGATGAACATGATGCCATCATTTAAGGAAATCCATGGACCAAGGATGGA
ATACAGATTGATGCTGCCCTATCAATTAATTGGTTATTAATAGTTAAAACAATATTCT
CTTTTGAAAATAGTATAAACAGGCCATGCATATAATGTACAGTGTATTACGTAAATATGTA
AAGATTCTCAAGGTAACAAGGGTTGGGTTGGAAATAAACATCTGGATCTTATAGACCGT
TCATACAATGGTTTAGCAAGTCATAGTAAGACAAACAAGTCCTATCTTTTTGGCT
GGGGTGGGGCATTGGTCACATATGACCAGTAATTGAAAGACGTCATCACTGAAAGACAGAA
TGCCATCTGGCATAAAATAAGAAGTTGTCACAGCACTCAGGATTTGGTATCTTTG
AGCTCACATAAGAACCTCAGTGCTTTCAGAGCTGGATATCTTAATTACTAATGCCACA
CAGAAATTATACAATCAAACATAGATCTGAAGCATAATTAAAGAAAACATCAACATTTTG
TGCTTAAACTGTAGTAGTTGGCTAGAAACAAACTCC

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FIGURE 298

MGLGARGAWAALLGTLQVLALLGAAHESAAMAASANIENGLPHNSSANSTETLQHVPSDH
TNETSNSTVKPPTSVASDSSNTVTTMKPTAASNTTPGMVSTNMTSTTLKSTPKTTSVSQN
TSQISTSTMVTNHNSVTSAASSVTITTMHSEAKKGSKFDTGSFVGGIVLTLGVLSILYIG
CKMYYSSRRGIRYRTIDEHDAII

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FIGURE 299

CAGCCGGGTCCCAAGCCTGTGCCTGAGCCTGAGCCTGAGCCGAGCCGGAGCCGG
TCGCAGGGCTCCGGCTGTGGGACCGCTGGCCCCCAGCG**ATGGC**GACCTGTGGGAGGC
CTTCTCGGCTTGGCTCCTGCTCAGCCTGCGCTGGCGCTTCCGTGCTGCTGCTGGC
GCAGCTGTAGACGCCAAGAATTGAGGATGTCAGATGAAATGTATCTGCCCTCC
ATAAAGAAAATTCTGGCATATTATAAGAACATATCTCAGAAAGATTGTGATTGCCTT
CATGTTGTGGAGCCATGCCTGTGCGGGGCTGATGTAGAACGATACTGTCTACGCTGTGA
ATGCAAATATGAAGAAAGAACGCTGTACAATCAAGGTTACCAATTATAATTATCTCTCCA
TTTGGGCCTTACTTGTACATGGTATATCTTACTCTGGTGGAGCCACTGAAGAGG
CGCCTTTGGACATGCACAGTTGATACAGAGTGATGATATTGGGGATCACCAGCCTT
TGCAAATGCACACGATGTGCTAGCCGCTCCCGCAGTCGAGCCAACGTGCTGAACAAGGTAG
AATATGCACAGCAGCGCTGGAAGCTTCAAGTCAAGAGCAGCGAAAGTCTGTCTTGACCGG
CATGTTGTCCCTCAGC**TAATT**GGGAATTGAATTCAAGGTGACTAGAAAGAACAGGCAGACAA
CTGGAAAGAACTGACTGGTTTGCTGGTTTCAACCTTGTGATTTCACCAACT
GTTGCTGGAAGATTCAAAACTGGAAGCAAAACTGCTTGATTTTTCTTGTAAACGTA
ATAATAGAGACATTTAAAGCACACAGCTAAAGTCAGCCAATAAGTCTTTCTATTG
TGACTTTACTAATAAAATAATCTGCCTGTAATTATCTGAAAGTCCTTACCTGGAACA
AGCACTCTCTTTTACACATAGTTAACCTGACTTCAAGATAATTTCAAGGTTTTG
TTGTTGTTGTTTGTGTTGTTGGGGAGAGGGGAGGGATGCCTGGGAAGTGGTT
AACAACTTTTCAAGTCACTTAAACAAACTTTGTAATAGACCTTACCTTCTATT
TCGAGTTTCAATTATTTGCAGTGTAGCCAGCCTCATCAAAGAGCTGACTTACTCATTG
ACTTTGCACTGACTGTATTATCTGGGTATCTGCTGTGCTGCACTTCATGGTAAACGGGAT
CTAAAATGCCTGGTGGCTTCAACAAAGCAGATTTCATGTACTGTGATGTCTGATG
CAATGCATCCTAGAACAAACTGCCATTGCTAGTTACTCTAAAGACTAACATAGTCTG
GTGTGTGTGGTCTTACTCATCTTAGTACCTTAAGGACAAATCTAAGGACTTGGACACT
TGCAATAAGAAATTATTTAAACCAAGCCTCCCTGGATTGATAATATACACATTG
TCAGCATTCCGGTGTGGTGGAGAGGCAGCTGTTGAGCTCCAATATGTGAGCTTGAAC
AGGGCTGGGTTGTGGTGCCTCTGAAAGGTCTAACCAATTATTGATAACTGGCTTTT
TCTTCCTATGTCCTTTGGAATGTAACAATAAAATAATTGAAACATCAA

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FIGURE 300

MATLWGGLRLGSLLSCLALSVLLAQLSDAAKNFEDVRCKCICPPYKENSGHIYNKNIS
QKDCDCLHVVEPMPVRGPDVEAYCLRCECKYEERSSVTIKVTIIIYLSILGLLLLYMYLTL
VEPILKRRLFGHAQLIQSDDDIGDHQPFANAHDLARSRSRANVLNKVEYAQQRWKLQVQEQR
RKSVFDRHVVL

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FIGURE 301

GCACCTGCGACCACCGTGAGCAGTCATGGCGTACTCCACAGTCAGAGAGTCGCTCTGGCTT
CTGGGCTTGTCCCTGGCTCTGTCGCTGCTGCCAAGGCCTCCTGTCCCAGGGAAAGCGG
CAGGAGCCGCCGCCGACACCTGAAGGAAAATTGGGCCGATTCCACCTATGATGCATCATCA
CCAGGCACCTCAGATGGCCAGACTCCTGGGCTCGTTCCAGAGGTCTCACCTGCCGAGG
CATTGCAAAGGCCAAGGATCAGGTGGAGGTGCTGGAGGAGGTAGTGGAAAGAGGTCTG
ATGGGGCAGATTATCCAATCTACGGTTGGGATTTTATATATACTGTACATTCTATT
TAAGGTAAGTAGAATCATCCTAATCATATTACATCAATGAAAATCTAATATGGCGATAAAA
TCATTGTCTACATTAAAATTCTTATAGTCATAAAATTATTCAAATCCATCATCTTTA
AATCCTGCCTCCTCTTCATGAGGTACTTAGGATAGCCATTATTCAGTTCACATAAGAATG
TTTACTCAATGTTAAGTGTGCCCCAAAATTACAACAAACAGGCAGAACTAGGACTT
GAACATGGATCTTGGTTCTTAATCCAGTGAGTGATAACAATTCAATGCACTCCCTGCCA

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FIGURE 302

MAYSTVQRVALASGLVLALSLLPKAFLSRGKRQEPPPTPEGKLGRFPPMMHHHQAPSDGQT
PGARFQRSHLAEAFAKAKGSGGAGGGGSGRGLMGQIIPYFGIFLYIYLIFKVSRIILI
ILHQ

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FIGURE 303

CGGCTCGAGTCAGCTGTGGGGAGATTCAGTGCATTGCCTCCCTGGGTGCTCTCATCTT
GGATTGAAAGTTGAGAGCAGCAGTGTTGCCACTGAAACTCATCCTGCTGCCAGTGTAC
TGGATTATTCCCTGGGCCTGAATGACTGAATGTTCCCGCTGAGCTAACAGTCCATGTG
GGTGATTCAAGCTCTGATGGATGTGTTCCAGAGCACAGAACAAATGTATATTCAAGAT
AGACTGGACTCTGTCAACCAGGAGAGCACGCCAAGGACGAATATGTGCTATACTATTACTCCA
ATCTCAGTGTGCCTATTGGCGCTTCCAGAACCGCGTACACTGATGGGGACATCTTATGC
AATGATGGCTCTCCTGCTCCAAGATGTGCAAGAGGCTGACCAGGGAACCTATATCTGTGA
AATCCGCCTCAAAGGGAGAGCCAGGTGTTCAAGAACGGCGGTGACTGCATGTGCTTCCAG
AGGAGCCCAAAGAGCTCATGGTCATGTGGTGGATTGATTGAGATGGATGTGTTCCAG
AGCACAGAAGTGAACACGTGACCAAGGTAGAATGGATATTCAGGACGGCGCGCAAAGGA
GGAGATTGTATTCGTTACTACCACAAACTCAGGATGTCTGGAGTACTCCCAGAGCTGG
GCCACTTCCAGAACATCGTGTGAACCTGGTGGGGACATTTCCGCAATGACGGTCCATCATG
CTTCAAGGAGTGAGGGAGTCAGATGGAGGAAACTACACCTGCAGTATCCACCTAGGAAACCT
GGTGTCAAGAAAACCATTGTGCTGCATGTCAGCCCGAACAGGCCTCGAACACTGGTGACCC
CGGCAGCCCTGAGGCCTCTGGTCTTGGTGGTAATCAGTTGGTGATCATTGTGGGAATTGTC
TGTGCCACAATCCTGCTGCTCCCTGTTCTGATATTGATCGTAAGAACAGACTGTGGAAATAA
GAGTTCAGTGAATTCTACAGTCTGGTGAAGAACACGAAGAACAGACTAATCCAGAGATAAAAG
AAAAACCTGCCATTGAAAGATGTGAAGGGAGAACACACATTACTCCCCAATAATTGTA
CGGGAGGTGATCGAGGAAGAACCAAGTGAAAATCAGAGGCCACCTACATGACCATGCA
CCCAGTTGGCCTCTGAGGTCAAGATCGAACACTCACTGAAAAAAAGTCAGGTGGGG
GAATGCCAAAAACACAGCAAGCCTTTGGAAGAACAGACTGTGCTCATCTCAGCAGCGG
TGGAGACTCTCCTGTGTGTCCTGGCCACTCTACAGTGATTCAGACTCCGCTCTC
CCAGCTGTCCTCTGTCATTGTTGGTCAATACACTGAAGATGGAGAACAGGCTGAGTGGACTTGGC
CAGAGAGACTGGACAGCTGGAGGAACAGGCCTGCTGAGGGAGGGAGCATGGACTTGGC
CTCTGGAGTGGACACTGGCCCTGGAACCCAGGCTGAGTGAGTGGCCTCAAACCCCCCGTT
GGATCAGACCCCTGTCAGGGTCTTAGTGGATGAGTTACTGGGAAGAACAGAGATA
AAAACCAACCAAATCAA

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FIGURE 304

MFCPLKLILLPVLLDYSLGLNDLNVSPPPELTVHVGDSALMGCVFQSTEDKCIFKIDWTLS
EHAKDEYVLYYYSNLSVPIGRFQNRVHLMGDILCNDGSLLLQDVQEADQGTYICEIRLK
QVFKKAVVLHVLPEEPKELMVHVGGLIQMGCVFQSTEVKHVTKVEWIFSGRR
AKEEIVFRYY
HKLRMSVEYSQSWSGHFQNRVNLVDIFRNDGSIMLQGVRESDG
GNYTC
SIHLGNLVFKKTIV
LHVSPEEPRTLVTPAALRPLVLGGNQLVIVGIVCAT
ILLPVLILIVKKTCGNKSSVN
STV
LVKNTKKTNPEIKEKPCHFERCEGEKHIYSPIIVREV
IEEEPSEKSEATYMTMHPVWPSLR
SDRNN
SLEKKSGGGMPKTQQAF

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FIGURE 305

CTATGAAGAAGCTTCCTGGAAAACAATAAGCAAAGGAAAACAAATGTGTCCCATCTCACATG
GTTCTACCCCTACTAAAGACAGGAAGATCATAAACTGACAGATACTGAAATTGTAAGAGTTGG
AAACTACATTTGCAAAGTCATTGAACCTGAGCTCAGTTGCAGTACTCGGAAAGCC**ATGCA**
GGATGAAGATGGATACTCACCTTAAATATTAAAACCTGGAAACCAGCTCTCGTCTCCGTG
GCCCTGCATCCTCCTGGTGGCGTGTGATGGCTTGATTCTGCTGATCCTGTGCGTGGGG
ATGGTTGTCGGCTGGTGGCTCTGGGATTGGTCTGTATGCAGCGCAATTACCTACAAGA
TGAGAATGAAAATCGCACAGGAACCTGCAACAATTAGCAAAGCGCTCTGTCAATATGTGG
TAAAACAATCAGAACTAAAGGGCACTTCAAAGGTATTAATGCAGCCCCTGTGACACAAAC
TGGAGATATTATGGAGATAGCTGCTATGGTTCTCAGGCACAACATTAACATGGGAAGAGAG
TAAGCAGTACTGCACTGACATGAATGCTACTCTCCTGAAGATTGACAACCGGAACATTGTGG
AGTACATCAAAGCCAGGACTCATTAATTCTGTTGGTCGGATTATCTGCCAGAAGTCGAAT
GAGGTCTGGAAGTGGGAGGATGGCTCGTTATCTCAGAAAATATGTTGAGTTTTGGAAGA
TGGAAAAGGAAATATGAATTGTGCTTATTTCATATAATGGGAAATGCACCCCTACCTCTGTG
AGAACAAACATTATTTAATGTGAGAGGAAGGCTGGCATGACCAAGGTGGACCAACTACCT
TAATGCACAGGAGGTGGACAGGATAACACAGATAAGGGTTATTGTACAATAAAAGATATGT
ATGAATGCATCAGTAGCTGAAAAAAAAAAAAAA

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FIGURE 306

MQDEDGYITLNKTRKPALSVGPASSSWWRVMALILLILCVGMVVGVLVALGIWSVMQRNYL
QDENENRTGTLQQLAKRFCQYVVKQSELKGTFKGHK CSPCDTNWRYYGDSCYGFFRHNLTWE
ESKQYCTDMNATLLKIDNRNIVEYIKARTHLIRWVGLSRQKSNEVWKWEDGSVISENMFEFL
EDGKGNMNCAYFHNGKMHPTFCENKHLMCERKAGMTKVDQLP

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FIGURE 307

CCACACGCGTCCGCGCAGTCGCGCAGTTCTGCCTCCGCCTGCCAGTCTCGCCCGCGATCCGG
CCCGGGCTGTGGCGTCGACTCCGACCCAGGCAGCCAGCAGCCCGCGCGGGAGCCGGACCGC
CGCCGGAGGAGCTCGGACGGCATGCTGAGCCCCCTCCTTGCTGAAGCCGAGTGCAGGAGAA
GCCCGGGAAACGCAGGCTAAGGAGACCAAAGCGGCGAAGTCGCGAGACAGCGGACAAGCAG
CGGAGGAGAAGGAGGAGGAGGCGAACCCAGAGAGGGGCAGCAAAAGAACGCGGTGGTGGTGG
CGTCGTGGCAATGGCGCGGCTATGCCAGCTCGCTCATCCGTCAGAACAGAGGCAAGCCCGCG
AGCGCGAGAAATCCAACGCCTGCAAGTGTGTCAGCAGCCCCAGCAAAGGCAAGACAGCTGC
GACAAAAACAAGTTAAATGTCTTTCCCGGTCAAACCTTCGGCTCCAAGAACAGAGGCGCAG
AAGAACGACAGAGCCTCAGCTTAAGGTATAGTTACCAAGCTATAACAGCCGACAAGGCTACC
ACTTGCAGCTGCAGGGGATGGAACCATTGATGGCACCAAAGATGAGGACAGCACTTACACT
CTGTTAACCTCATCCCTGTGGGTCTGCGAGTGTTGGCTATCCAAGGAGTTCAAACCAAGCT
GTACTTGGCAATGAACAGTGAGGGATACTTGTACACCTCGGAACCTTCACACCTGAGTGCA
AATTCAAAGAACAGTGTGAAATTATTATGTGACATATTCAATGATATACCGTCAG
CAGCAGTCAGGCCGAGGGTGGTATCTGGGTCTGAACAAAGAACAGGAGAGATCATGAAAGGCAA
CCATGTGAAGAACACAAGCCTGCAGCTCATTCTGCCTAAACCAACTGAAAGTGGCCATGT
ACAAGGAGCCATCACTGCACGATCTCACGGAGTTCTCCGATCTGGAACGCCGACAAATGAATCAAC
AAGAGCAGAAGTGTCTCTGGCGTGTGAACGGAGGCAAATCCATGAGCCACAATGAATCAAC
G**TAG**CCAGTGAGGGAAAGAACAGGCTCTGTAACAGAACCTTACCTCCAGGTGCTGTTGAAT
TCTTCTAGCAGTCCTCACCCAAAAGTTCAAATTGTCAGTGACATTACCAAACAAACAGG
CAGAGTTCACTATTCTATCTGCCATTAGACCTTATCATCCATACTAAAGC

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FIGURE 308

```
></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA28498
><subunit 1 of 1, 245 aa, 1 stop
><MW: 27564, pI: 10.18, NX(S/T): 1
MAAAIASSLIQRQAREREKSACKCVSSPSKGKTSCDKNKNLNVFSRVKLFGSKKRRRRP
EPQLKGIVTKLYSRQGYHLQLQADGTIDGKDEDSTYTLFNLIPVGLRVVAIQGVQTKLYLA
MNSEGYLYTSELFPECKFKEVFENYYVTYSSMIYRQQQSGRGWYLGLNKEGEIMKGNHVK
KNKPAAHFLPKPLKVAMYKEPSLHDLTEFSRSGSGTPTKSRSGVNLNGGKSMHNEST
```

N-glycosylation site.

amino acids 242-246

Glycosaminoglycan attachment site.

amino acids 165-169, 218-222

Tyrosine kinase phosphorylation site.

amino acids 93-100

N-myristoylation site.

amino acids 87-93, 231-237

ATP/GTP-binding site motif A (P-loop).

amino acids 231-239

HBGF/FGF family proteins

amino acids 78-94, 102-153

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FIGURE 309

CCAGGATGGAGCTGGGCCTGTATGCCATTATTGTTCTATGCTACTAGACATGGGGGG
ACTTGGTAAAAAGGTATTATCAGCCAGAGGGCTGGAGGCCGTCTTACTGAACCTGG
CAACCTGGATATTCTGAGACATATTGGGGGATTCAGTAAAAAGTGGGGATCCC
CCATTTAGAGTGTAGCAAAGGAAAAACACCAAGGTTGGGTCCTCCTGACATTGGCAGTG
CCCCAGTAGGGTGGGATGAGCGAATATTCCAAAGCTAAAGTCCCACACCCTGTAGATTAC
AAGAGTGGATTGGCAGGAGTGTGCCCAAAATACAGTGGAAAGGTGCCTGAAGATATTAA
ACCACGTCTGGAAATTAGTGGTCTTGGCTTGGATAGGTGAAGTGAGGACAGACACTG
GAGAGGAGGGAAAGGGGACGTTCAATAGGAGGAAAACCTCGAGGGTGGATCCACTGAGG
AGTACATAGGCTGCTGGATCTGGTGGAGCCAGCACTGGGCCACGGTGGTAAGTGGCTGCT
GTGGAGGGGGTACGTGAGGGGGGGTCTGGGCTTATCCTCAGGTCTGTGGTGGGCAG
CGAGTCGGGCCTGAGCGTAAGAGCATGCCCTAGTGAGCGGGCTCCTCTGGGGAGCCCAG
CGCGCTCCGGCGCCTGCCGGTTGGGGTGTCTCCTCCCAGGCGCTGGCAGCCGGCGTGTGG
CAGTAGCCTGATCCGGCAGAAGCGGGAGGTCCCGAGCCCAGGGCAGCCGGCGTGTGG
CGCAGCGCGCGTGTGTCCCCCGGCACCAAGTCCCTTGCCAGAAGCAGCTCCTCATCCTG
CTGTCCAAGGTGCGACTGTGCGGGGGCGGCCGCGCCGGACCGCGCCGGAGCCTCA
GCTCAAAGGCATCGTACCAAACTGTTCTGCCGCCAGGGTTCTACCTCCAGGGAATCCCG
ACGGAAGCATCCAGGGCACCCCAGAGGATACCAAGCTCCTCACCCACTCAACCTGATCCCT
GTGGGCCTCCGTGTGGTCACCATCCAGAGCGCAAGCTGGTCACTACATGGCATGAATGC
TGAGGGACTGCTTACAGTTCGCCGCATTACAGCTGAGTGTGCTTAAGGAGTGTGTCT
TTGAGAATTACTACGTCCTGTACGCCCTGCTCTACCGCCAGCGTCGTTCTGGCGGGCC
TGGTACCTCGGCCTGGACAAGGAGGGCAGGTATGAAGGAAACCGAGTTAAGAAGACCAA
GGCAGCTGCCACTTCTGCCAAGCTCCTGGAGGTGGCATGTACCAGGAGCCTCTCC
ACAGTGTCCCCGAGGCCTCCCCCTCCAGTCCCCCTGCCCCCTGAAATGTAGTCCCTGGACTG
GAGGTTCCCTGCACTCCAGTGAAGCCAGCCACCACAAACCTGT

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FIGURE 310

MAALASSLIRQKREVREPAGSRPVSAQRRVCPRGKSLCQKQLLILLSKVRLLCGGRPARPDR
GPEPQLKGIVTKLFCRQGFYLQANPDGSIQGTPEDTSSFTHFNLIPVGLRVVTIQSAKLGHY
MAMNAEGLLYSSPHFTAECRFKECVFENYYVLYASALYRQRRSGRAWYLGLDKEGQVMKGNR
VKKTAAAHLPLKLLLEVAMYQEPQLHSVPEASPSSPPAP

Tyrosine kinase phosphorylation site:

amino acids 199-207

N-myristoylation sites:

amino acids 54-60, 89-95, 131-137

HBGF/FGF family signature:

amino acids 131-155

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FIGURE 311

ATGGCCGCCATCGCTAGCGGTTGATCCGCCAGAACGGCAGGCCGGAGCAGCACTGGACCGCCGCTCTGCAACGGACACCTGGTGGATATCTTCTCAAAGTGCGCATCTTCGGCCTCAAGAACGCGCAGGTTGCCGCAGCAAGGCTACTACTTGCACAAATGCACCCCGATGGAGCTCTCGATGGAACCAAGGATGACAGCACTAATTCTACACTCTAACCTCATACCAGTGGGACTACGTGTTGCCATCCAGGGAGTAAAACAGGGTTGTATATAGCCATGAATGGAGAAGGTTACCTCTACCCATCAGAACTTTTACCCCTGAATGCAAGTTTAAAGAATCTGTTTGAAAATTATTATGTAATCTACTCATCCATGTTGTACAGACAACAGGAATCTGGTAGAGCCTGGTTGGATTAAATAAGGAAGGGCAAGCTATGAAAGGGAACAGAGTAAAGAAAACCAAACCAAGCAGCTCATTTCTACCCAAGCCATTGGAAGTTGCCATGTACCGAGAACCATCTTGCATGATGTTGGGAAACGGTCCCGAAGCCTGGGTGACGCCAAGTAAAAGCACAAAGTGCCTGCAATAATGAATGGAGGCAAACCAAGTCAACAAAGAGTAAGACAACATAG

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FIGURE 312

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></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA28503
><subunit 1 of 1, 247 aa; 1 stop
><MW: 27702, pI: 10.36, NX(S/T): 2
MAAAIASGLIRQKRQAREQHWDRPSASRRSSPSKNRGLCNGNLVDIFSKVRIFGLKKRRLR
RQDPQLKGIVTRLYCRQGYYLQMHPDGALDGTDDDSTNSTLFNLIPVGLRVVAIQGVKTGLY
IAMNGEGLYPSELFTEPECKFKESVFENYYVIYSSMLYRQQESGRAWFLGLNKEGQAMKGNR
VKKTKPAAHFLPKPLEVAMYREPSLHDVGETVPKPGVTPSKSTSASAIMNGGKPVNKSKTT
```

N-glycosylation site.

amino acids 100-104, 242-246

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 28-32, 29-33

Tyrosine kinase phosphorylation site.

amino acids 199-207

N-myristoylation site.

amino acids 38-44, 89-95, 118-124, 122-128, 222-228

HBGF/FGF family proteins.

amino acids 104-155, 171-198

FIGURE 313

GGGGAGAGGAATTGACCATGTAAAAGGAGACTTTTTTTGGTGGTGGCTGTTGGGTGCCTGC
AAAGGATGCAGGACGCAGCTTCTCTGGAACCGAACGCAATGGATAACTGATTGTGCAAGAGAGAACGAGA
ACGAAGCTTTCTTGTGAGCCCTGGATCTAACACAAATGTGTATATGTGACACACAGGGAGCATTCAAGAATG
AAATAAACCAGAGTTAGACCCGCGGGGTTGGTGTGTTCTGACATAAATAATCTAAAGCAGCTGTTCCC
CTCCCCACCCCCAAAAAAAGGATGGAAATGAAGAACCGAGGATTACAAAGAAAAAGTATGTTCATTT
TTCTCTATAAAGGAGAAAGTGGAGGAGATATTTGGAAATGAAAAGTTGGGCTTTTAGTAAAGTAA
AGAACTGGTGTGGTGGTGTTCCTTCTTTGAATTCCCACAAGAGGAGAGGAATTAAATAACATCTGC
AAAGAAATTCAGAGAAGAAAAGTGGACCGCGCAGATTGAGGCATTGATTGGGGAGAGAACACAGCAGAGCA
CAGTTGGATTTGCGCTATGTTGACTAAATTGACGGATAATTGAGCTGGATTTCTTCATCAACCTCCTT
TTTTAAATTTTATTCCCTTGGTATCAAGATCATGCGTTCTTGTCTTAACCACCTGGATTTCATCT
GGATGTTGCTGTGATCAGTCTGAAATACAACACTGTTGAATTCCAGAACCCAGATAAATTATGAATG
TTGAACAAGATGACCTTACATCCACAGCAGATAATGATAGGCTCTAGGTTAACAGGGCCCTATTGACCCCT
GCTTGTGGTGTGCTGGCTCTTCAACTCTTGTGGTGGCTGGTCTGGTGGGGCTCAGACCTGCCCTGTG
GCTCCTGCAGCAACCAGTCAGCAAGGTGATTGTTGCGAAAAACCTGCGTGAGGTTCCGGATGGCATCTCC
ACCAACACACGGCTGCTGAACCTCCATGAGAACCAAATCCAGATCATCAAAGTGAACAGCTCAAGCACTGAG
GCACTGGAAATCCTACAGTTGAGTAGGAACCATATCAGAACCCATTGAAAGCATCCCTCTTATGCTTTCA
CTGAAGGAGCTGGTGCAGAACCCATTGAAAGCATCCCTCTTATGCTTTAACAGAACCCATTGAG
GCCTGGCAACTAGACTGGGAAATGAAAAGACTTTCATACATCTCAGAACGGTGCCTTGAAGGCTGTCAACT
TGAGGTATTGAAACCTTGCATGTGCAACCTCAGGAAATCCCTAACCTCACACCGCTCATAAA
ACTAGATGAGCTGGATCTTCTGGGAATCATTTATCTGCCATCAGGCCCTGGCTTTCCAGGGTTGATGCACCT
GTGGATGATACTCCCAGATTCAACTGATTGAAACGGATGCCCTTGACAACCTTCAGTCAGTCAGTGAG
ACCTGGCACACATAATCTAACATTACTGCCTCATGACCTCTCACTCCCTGCATCATCTAGAGCGGAC
ACATTTGACACCCATTGGAACCTGTAACACTGTTGACATACTGTGGCTCAGCTGGTGGATAAAAGAC
ATGGCCCCCTCAGACAGCTTGTGCCCCGGTGTAAACACTCCTCCAACTCTAAAGGGGAGGTACATTGG
GAGCTGAAATGCGGGCCTCCACATCCCTGACATCTGTATCTGGATTACTCCAAATGGAACAGTCAG
GACACACGCTTGTGCCCCGGTGTAAACACTCCTCCAACTCTAAAGGGGAGGTACATTGGAGAGCTGACC
ATTACTTCACATGCTATGTCCTGGTGTGAGGAGGCCCCCTGCAGACCTCAATGTCAGTCAGGATGGCAG
GAGCTGAAATGCGGGCCTCCACATCCCTGACATCTGTATCTGGATTACTCCAAATGGAACAGTCAG
GACACACGCTTGTGCCCCGGTGTAAACACTCCTCCAACTCTAAAGGGGAGGTACATTGGAGAGCTGACC
GCAACCAACTCCTTCTTACTTTCAACCGTCACAGTAGAGACTATGGAACCGTCTCAGGATGAGGCAC
GACACAGATAACATGTGGTCCCACCTCCAGTGTGACTGGAGACCACCAATGTGACCCACCTCTCACAC
CACAGAGCACAAGGTCGACAGAGAAAACCTCACCACCCAGTGACTGATATAAACAGTGGGATCCCAGGAATT
GATGAGGTGATGAAGACTACCAAAATCATCATTGGTGTGTTGTGCCATCACACTCATGGCTGCAGTG
GGTCATTTCTACAAGATGAGGAAGCAGCACCAGCGAACACCCATCAGGCCCAACAGGACTGTTGAAATT
TTAATGTGGATGAGATTACGGAGACACCCATGGAAAGCCACCTGCCATGCCTGCTATCGAGCATGAG
CACCTAAATCACTATAACTCATACAAATCTCCCTCAACCACACAACAGTTAACACAATAATTCAATACA
CAGTCAGTGCATGAACCGTTATTGATCCGAATGAACTCTAAAGACAAATGTACAAGAGACTCAA
TTTACAGAGTTACAAAAACAAATCAAAAAAAAGACAGTTATTAAAATGACACAAATGACTGGCTAA
ATCTACTGTTCAAAAAAGTGTCTTACAAAAAAACAAAAAGAAAAGAAATTATTATTAAAAATTCTATTG
TGATCTAAAGCAGACAAAAA

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FIGURE 314

MLNKMTLHPQQIMIGPRFNRALFDPLLVLLALQLLVVAGLVRAQTCPSVCSCSNQFSKVIC
VRKNLREVPDGISTNTRLLNLHENQIQIICKVNSFKHLRHEILQLSRNHIRTIEIGAFNGLA
NLNTLELFDNRLTTIPNGAFVYLSKLKELWLRNNPIESIPSYAFNRIPLRRLDLGELKRLS
YISEGAFEGLSNLRYILNLAMCNLREIPNLPLIKLDELDLSGNHLSAIRPGSFQGLMHLQKL
WMIQSQIQVIERNNAFDNLQSLVEINLAHNNLTLPHDLFTPPLHHLERIHLHHNPWCNCDIL
WLSWWIKDMAPSNTACCARCNTPPNLKGRYIGELDQNYFTCYAPVIVEPPADLNVTGMAAE
LKCRASTSLTSVSWITPNGTVMTHGAYKVRIAVLSDGTLNFTNVTVQDTGMYTCMVSNSVGN
TTASATLNVTAATTPFSYFSTVTVETMEPSQDEARTTDNNVGPTPVVDWETTNVTTSLTPQ
STRSTEKTFITPVTDINSGIPGIDEVMKTTKIIIGCFVAITLMAAVMLVIFYKMRKQHHRQN
HHAPTRTVEIINVDEITGDTPMESHLPMPAIEHEHLNHYNSYKSPFNHTTVNTINSIHSS
VHEPLLIRMMNSKDNVQETQI

Signal sequence:

amino acids 1-44

Transmembrane domain:

amino acids 523-543

N-glycosylation site.amino acids 278-282, 364-368, 390-394, 412-416, 415-419,
434-438, 442-446, 488-492, 606-610**cAMP- and cGMP-dependent protein kinase phosphorylation site.**

amino acids 183-187

Casein kinase II phosphorylation site.

amino acids 268-272, 417-421, 465-469, 579-583, 620-624

N-myristoylation site.amino acids 40-46, 73-79, 118-124, 191-197, 228-234, 237-243,
391-397, 422-428, 433-439, 531-537

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FIGURE 315

GC GCC GGG AGCCC AT CTGCC CAGGGG CACGGG CGCGGG CGCTCCGCCGGCACAT
GGCTGCAGCCACCTCGCGCACCCGAGGCAGCGCCAGCTCGCCCGAGGTCCGTGGA
GGCGCCCGGCCGCCCGAGCCAAGCAGCAACTGAGCGGGGAGCGCCCGCGTCCGGGATC
GGGATGTCCCTCCTCTCTGCTAGTTCTACTATGTTGGAACCTTGGGACTCA
CACTGAGATCAAGAGAGTGGCAGAGGAAAAGGTCACTTGCCTGCCACCATCAACTGGGC
TTCCAGAAAAGACACTCTGGATATTGAATGGCTGCTACCGATAATGAAGGGAACCAAAA
GTGGTGATCACTTACTCCAGTCGTATGTCTACAATAACTTGACTGAGGAACAGAAGGGCG
AGTGGCCTTGCTTCCAATTCTGGCAGGAGATGCCTCCTGCAGATTGAACCTCTGAAGC
CCAGTGATGAGGGCCGGTACACTGTAAGGTTAAGAATTCAAGGGCGCTACGTGTGGAGCCAT
GTCATCTAAAAGTCTTAGTGAGACCATCCAAGCCAAGTGTGAGTTGGAAGGAGAGCTGAC
AGAAGGAAGTGACCTGACTTGCAGTGTGAGTCATCCTCTGGCACAGAGCCATTGTGTATT
ACTGGCAGCGAATCCGAGAGAAAAGAGGGAGAGGATGAACGTCTGCCTCCAAATCTAGGATT
GAECTACAACCACCTGGACGAGTTCTGCTGCAGAACTTACCATGTCTACTCTGGACTGTA
CCAGTGACAGCAGGAACGAAGCTGGGAAGGAAAGCTGTGTGGTGCAGTAACTGTACAGT
ATGTACAAAGCATCGGCATGGTGCAGGAGCAGTGACAGGCATAGTGGCTGGAGCCCTGCTG
ATTTCTCTGGTGTGGCTGTAATCCGAAGGAAAGACAAAGAAAGATATGAGGAAGAAGA
GAGACCTAATGAAATTGAGAAGATGCTGAAGCTCAAAGCCGCTTGTGAAACCCAGCT
CCTCTCTCAGGCTCTCGGAGCTCACGCTCTGGTTCTCCACTCGCTCCACAGCAAAT
AGTGCCTCACGCAGCCAGCGGACACTGTCAACTGACGCAGCACCCAGCCAGGGCTGCCAC
CCAGGCATAACGCCTAGTGGGCCAGAGGTGAGAGGTTCTGAACCAAAGAAAGTCCACCATG
CTAATCTGACCAAAGCAGAAACCACACCAGCATGATCCCCAGCCAGAGCAGAGCCTTCCAA
ACGGTC**TGA**ATTACAATGGACTGACTCCCACGCTTCTAGGAGTCAGGGTCTTGGACTC
TTCTCGTATTGGAGCTCAAGTCACCAGCCACACAACCAGATGAGAGGTCATCTAAGTAGCA
GTGAGCATTGCACGGAACAGATTAGCAGATGAGCATTTCCTTACAATACCAAACAAGCAA
AGGATGTAAGCTGATTCACTGTAAGGATCTTATTGTGCTTCTAGACCAGAGTAAGGG
AAAGCAGGAGTCCAAATCTATTGTTGACCAGGACCTGTGGTGAAGGTTGGGAAAGGTG
AGGTGAATATACCTAAAACCTTTAATGTGGATATTGTATCAGTGTCTTGATCACAATT
TTCAAGAGGAATGGGATGCTTTGTAATTTCTATGCAATTCTGCAAACCTATTGGATT
ATTAGTTATTCAAGACAGTCAGCAGAAACCCACAGCCTTATTACACCTGTCTACACCATGTAC
TGAGCTAACCACTCTAACGAAACTCCAAAAAGGAAACATGTGTCTTCTATTCTGACTTAAC
TTCATTGTCATAAGGTTGGATATTCAAGGGAGTGAAATAGTGGAGATGGAGA
AGAGTGAATGAGTTCTCCACTCTATAACTAATCTCACTATTGTATTGAGCCAAAATAAC
TATGAAAGGAGACAAAAATTGTGACAAAGGATTGTGAAGAGCTTCCATCTCATGATGTT
ATGAGGATTGTGACAAACATTAGAAATATATAATGGAGCAATTGTGGATTCCCTCAAAT
CAGATGCCTCTAACGGACTTCTGCTAGATATTCTGGAAGGAGAAAATACAACATGTCAATT
TATCAACGTCCTTAGAAAGAATTCTCTAGAGAAAAAGGGATCTAGGAATGCTGAAAGATTA
CCCAACATACCAATTATAGTCTCTTCTGAGAAAATGTGAAACCAGAATTGCAAGACTGG
GTGGACTAGAAAGGGAGATTAGATCAGTTCTCTTAATATGTCAAGGAAGGTAGCCGGCA
TGGTGCAGGCACCTGTAGGAAAATCCAGCAGGTGGAGGTTGCAGTGAGCCGAGATTATGCC
ATTGCACTCCAGCCTGGGTGACAGAGCGGGACTCCGTCTC

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FIGURE 316

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA45419
><subunit 1 of 1, 373 aa, 1 stop
><MW: 41281, pI: 8.33, NX(S/T): 3
MSLLLLLLVSYYVGTGHTEIKRVAEEKVTLPCHHQLGLPEKDTLDIEWLLTDNEGNQKV
VITYSSRHVYNNLTEEQKGRVAFASNFLAGDASLQIEPLKPSDEGRYTCKVKNSGRYVWSHV
ILKVLVRPSKPCKELEGELTEGSDLTLQCESSSGTEPIVYYWQRIREKEGEDERLPPKSRID
YNHPGRVLLQNLTMYSGLYQCTAGNEAGKESCVVRVTVQYVQSIGMVAGAVTGIVAGALLI
FLLVWLLIRRKDKERYEEEERPNEIREDAEAPKARLVKPSSSSGSRSSRSGSSSTRSTANS
ASRSQRTLSTDAAAPQPLATQAYSLVGPEVRGSEPKVHHANLTKAETTPSMIPSQSRAFQTV
```

Signal sequence:

amino acids 1-16

Transmembrane domain:

amino acids 232-251

FIGURE 317

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FIGURE 318

```
></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA82361
><subunit 1 of 1, 352 aa, 1 stop
><MW: 38938, pI: 7.86, NX(S/T): 3
MALLLCFVLLCGVVDFARSLSITTPPEEMIEKAKGETAYLPCKFTLSPEDQGPLDIEWLISPA
DNQKVDQVILYSGDKIYDDYPDLKGRVHFTSNDLKSGDASINVNLQLSDIGTYQCKVKK
APGVANKKIHVVLVKPSGARCYVDGSEEIGSDFKIKCEPKE GSLPLQYEWQKLSDSQKMPT
SWLAEMTSSVISVKNASSEYSGTYSCTVRNRVGSDQCLLRLNVVPPSNKAGLIAGAIIGTLL
ALALIGLIIFCCRKKRREEKYKEVHDIRDVPPPKSRTSTARSYIGSNHSSLGSMSPSNM
EGYSKTQYNQVPSEDFERTPQSPTLPPAKFKYPYKTDGITVV
```

Signal sequence.

amino acids 1-19

Transmembrane domain:

amino acids 236-257

N-glycosylation sites.

amino acids 106-110, 201-205, 298-302

Tyrosine kinase phosphorylation sites.

amino acids 31-39, 78-85, 262-270

N-myristoylation sites.

amino acids 116-122, 208-214, 219-225, 237-243, 241-247,
245-251, 296-302

Myelin P0 protein.

amino acids 96-125

FIGURE 319

TGAAATGACTTCCACGGCTGGACGGAACCTCCACCCACAGCTATGCCTCTGATTGGTGA
ATGGTGAAGGTGCCTGTCTAACCTTCTGAAAAAGAACCGAGCTGCCTCCAGGCAGCCAGCC
CTCAAGCATCACTTACAGGACCAGAGGGACAAGACATGACTGTGATGAGGAGCTGCTTCGC
CAATTAAACACCAAGAAGAATTGAGGCTGCTGGAGGAAGGCCAGGAGGAACACGAGACTG
AGAGATGAATTTCAACAGAGGCTGCAAAGCCTGTGGACTTAGCCAGACCCTCTGCCCTC
CTTGCTGGCGACAGCCTCTCAAATGCAGATGGTGTGCTCCCTGCCTGGTTTACCCCTG
CTTCTCTGGAGCCAGGTATCAGGGCCAGGGCCAAGAATTCCACTTGGGCCCTGCCAAGT
GAAGGGGTTGTTCCCCAGAAACTGTGGGAAGCCTCTGGCTGTGAAAGACACTATGCAAG
CTCAGGATAACATCACGAGTGCCCGGCTGCTGCAGCAGGAGGTTCTGCAGAACGTCCTGGAT
GCTGAGAGCTGTTACCTTGTCCACACCCCTGCTGGAGTTCTACTTGAAAATGTTCAAAAA
CCACCACAATAGAACAGTTGAAGTCAGGACTCTGAAGTCATTCTACTCTGCCAACAACT
TTGTTCTCATCGTGTACAACGTGCAACCCAGTCAAGAAAATGAGATGTTCCATCAGAGAC
AGTGCACACAGGCAGGTTCTGCTATTCCGGAGAGCATTCAAACAGTTGGACGTAGAACGAGC
TCTGACCAAAGCCCTGGGAAGTGGACATTCTCTGACCTGGATGCAGAAATTCTACAAGC
TCTGAATGTCAGACCAGGACCTCCCTCCCCCTGGCACTGGTTGTTCCCTGTGTCATTC
AACAGTCTCCCTCCTATGCTGTTCACTGGACACTTCACGCCCTGGCATGGTCCCATTC
TTGGCCCAAGGATTATTGTCAAAGAACGTCATTCTTAAGCAGCGCCAGTGACAGTCAGGGAAAG
GTGCCTCTGGATGCTGTGAAGAGTCTACAGAGAACGATTCTGTATTTATTACAACACTTATT
AATTAATGTCAGTATTCAACTGAAGTTCTATTATTGTGAGACTGTAAGTTACATGAAGG
CAGCAGAATATTGTGCCCATGCTTCTTACCCCTCACAACTCCTGCCACAGTGTGGGCAG
TGGATGGGTGCTTAGTAAGTACTTAATAAAACTGTGGTGCTTTGGCCTGTCTTGGATT
GTTAAAAAAACAGAGAGGGATGCTGGATGTAACACTGAACTCAGAGCATGAAATCACACT
GTCTTCTGATATCTGCAGGGACAGAGCATTGGGTGGGGTAAGGTGCATCTGTTGAAAAG
TAAACGATAAAATGTGGATTAAAGTGCCAGCACAAAGCAGATCCTCAATAAACATTCATT
TCCCACCCACACTGCCAGCTCACCCATCATCCCTTCCCTGGTGCCCTCCTTTTT
TATCCTAGTCATTCTCCCTAATCTTCCACTTGAGTGTCAAGCTGACCTGCTGATGGTGAC
ATTGCACCTGGATGTACTATCCAATCTGTGATGACATTCCCTGCTAATAAAAGACAACATAA
CTCCAAAAAAAAAAAAAAAAAAAAAA

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FIGURE 320

```
></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA88002
><subunit 1 of 1, 206 aa, 1 stop
><MW: 23799, pI: 9.12, NX(S/T): 3
MNFQQRLQSLWTLARPFCPPLLATASQMQMVLPCLGFTLLLWSQVSGAQGQEFGFGPCQVK
GVVPQKLWEAFWAVKDTMQAQDNITSARLLQQEVLQNVSDAESCYLVHTLLEFYLKTVFKNH
HNRTVEVRTLKSFSTLANNFVLIVSQLQPSQENEMFSIRDSAHRRFLLFRRAFKQLDVEAAL
TKALGEVDILLTWMQKFYKL
```

Signal sequence:

amino acids 1-42

N-glycosylation sites.

amino acids 85-89, 99-103, 126-130

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FIGURE 321

AAGGAGCAGCCCGCAAGCACCAAGTGAGAGGCATGAAGTTACAGTGTGTTCCCTTGGCTC
CTGGGTACAATACTGATATTGTGCTCAGTAGACAACCACGGTCTCAGGAGATGTCTGATTTC
CACAGACATGCACCATAAGAAGAGAGTTCCAAGAAATCAAAGAGCCATCCAAGCTAAGG
ACACCTCCAAATGTCACTATCCTGTCACATTGGAGACTCTGCAGATCATTAAGCCCTTA
GATGTGTGCTGCGTGACCAAGAACCTCCTGGCGTTCTACGTGGACAGGGTGTCAAGGATCA
TCAGGAGCCAAACCCAAAATCTTGAGAAAATCAGCAGCATTGCCAACTCTTCCTCTACA
TGCAGAAAACCTGCGGCAATGTCAGGAACAGAGGCAGTGTCACTGCAGGCAGGAAGCCACC
AATGCCACCAAGAGTCATCCATGACAACATGATCAGCTGGAGGTCCACGCTGCTGCCATTAA
ATCCCTGGGAGAGCTCGACGTCTTCTAGCCTGGATTAATAAGAATCATGAAGTAATGTTCT
CAGCTTGATGACAAGGAACCTGTATAGTGATCCAGGGATGAACACCCCTGTGCGGTTACT
GTGGGAGACAGCCCACCTTGAGGGGAAGGGAGATGGGGAAAGGCCCTTGAGCTGAAAGTCC
CACTGGCTGGCCTCAGGCTGTCTTATTCCGCTTGAAAATAGGCCAAAGTCTACTGTGGTAT
TTGTAATAAACTCTATCTGCTGAAAGGGCTGCAGGCCATCCTGGAGTAAAGGGCTGCCTT
CCCATCTAATTTATTGTAAAGTCATATAGTCATGTGATGTGAGCCAAGTGATATCCT
GTAGTACACATTGTACTGAGTGGTTTCTGAATAAATTCCATATTTACCTATGA

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FIGURE 322

></usr/seqdb2/sst/DNA/Dnaseqs.full/ss.DNA92282
><subunit 1 of 1, 177 aa, 1 stop
><MW: 20452, pI: 8.00, NX(S/T): 2
MKLQCVSLWLLGTILILCSVDNHGLRRCLISTDMHHIEESFQEIKRAIQAKDTFPNVTILST
LETLQIIKPLDVCCVTKNLLAFYVDRVFKDHQEPNPKILRKISSIANSFLYMQKTLRQCQEQRQCHCRQEATNATRVIHDNYDQLEVHAAAIKSLGELDVFLAWINKNHEVMFSA

Signal sequence:

amino acids 1-18

N-glycosylation sites.

amino acids 56-60, 135-139

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 102-106

N-myristoylation site.

amino acids 24-30

Actinin-type actin-binding domain signature 1.

amino acids 159-169

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FIGURE 323

CCCGTGCCAAGAGTGACGTAAGTACCGCCTATAGAGTCTATAGGCCACTGGCTTCGTTAG
AACGCGGCTACAATTAATACATAACCTTATGTATCATACACATACGATTAGGTGACACTAT
AGAATAACATCCACTTGCCTTCTCTCACAGGTGTCCACTCCCAGGTCCAACTCACCTC
GGTTCTATCGATAATCTCAGCACCCAGCCACTCAGAGCAGGGCACGATGTTGGGGCCCGCCT
CAGGCTCTGGGTCTGTGCCTTGTGCAGCGTCTGCAGCATGAGCGTCCTCAGAGCCTATCCA
ATGCCTCCCCACTGCTCGGCTCCAGCTGGGTGGCCTGATCCACCTGTACACAGCCACAGCC
AGGAACAGCTACCACCTGCAGATCCACAAGAATGCCATGTGGATGGCACCACAGAC
CATCTACAGTGCCTGATGATCAGATCAGAGGATGCTGGCTTGTGGTATTACAGGTGTGA
TGAGCAGAAGATACTCTGCATGGATTCAAGAGGCAACATTGGATCACACTATTCGAC
CCGGAGAACTGCAGGTTCCAACACCAGACGCTGGAAAACGGGTACGACGTCTACCACTCTCC
TCAGTATCACTCCTGGTCAGTCTGGCCGGCGAAGAGAGGCCTTCTGCCAGGCATGAACC
CACCCCCGTACTCCCAGTCCCTGTCCCGAGGAACGAGATCCCCCTAATTCACTTCAACACC
CCCATACCACGGCGGCACACCCGGAGCGCCGAGGACGACTCGGAGCGGGACCCCTGAACGT
GCTGAAGCCCCGGGCGGATGACCCCGCCCGCCCTGTCACAGGAGCTCCCGAGCG
CCGAGGACAACAGCCCGATGGCCAGTGACCCATTAGGGTGGTCAGGGCGGTGAGTGAAC
ACGCACGCTGGGAAACGGGCCGGAAGGCTGCCGCCCTCGCCAAGTTCATCTAGGTCG
CTGG

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FIGURE 324

```
></usr/seqdb2/sst/DNA/Dnaseqs.min/ss.DNA142238
><subunit 1 of 1, 251 aa, 1 stop
><MW: 27954, pI: 9.22, NX(S/T): 1
MLGARLRLWVCALCSVCSMSVLRAYPNASPLLGSSWGGLIHLHYTATARNSYHLQIHKNGHVD
GAPHQTIYSALMIRSEDAGFVVITGVMSSRYLCMDFRGNIFGSHYFDPENCRFQHQTLENGY
DVYHSPQYHFLVSLGRAKRAFLPGMNPPPSQFLSRRNEIPLIHFNTPIPRRHTRSAEDDSE
RDPLNVLKPRARMTPAPASCSQELPSAEDNSPMASDPLGVVRGGRVNTHAGGTGPEGCRPFA
KFI
```

Important features of the protein:**Signal peptide:**

amino acids 1-24

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 175-179

N-myristoylation site.

amino acids 33-39, 100-106, 225-231, 229-235

HBGF/FGF family proteins

amino acids 73-124

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FIGURE 325

GGAAAAGGTACCGCGAGAGACAGCCAGCAGTTCTGTGGAGCAGCGGTGGCCGGCTAGG**ATG**
GGCTGTCTCTGGGTCTGGCTCTGCCCTTTCTTCTGCTGGAGGTTGGGGCTCTGG
GAGCTCTGCAGGCCAGCACCCAGCAGACACTGCGATGACAACGGACGACACAGAAG
TGCCCGCTATGACTCTAGCACCGGCCACGCCGCTCTGAAACTCAAACGCTGAGCGCTGAG
ACCTCTCTAGGGCCTCAACCCAGCCGCCATTCCAGAAGCAGAGACCAGGGAGCAA
GAGAATTCCCCTGCAAGAGAGACCAGGAGTTACAAAAACATCTCCAACTTCATGGTGC
TGATGCCACCTCCGTGGAGACATCAGCCGCCAGTGGCAGGCCAGGGAGCTGGAATGACC
ACAGTTCAGACCATCACAGGCAGTGATCCCAGGAAGCCATTTGACACCCTTGCACCGA
TGACAGCTCTGAAGAGGCAAAGACACTCACAATGGACATATTGACATTGGCTCACACCTCCA
CAGAAGCTAAGGGCCTGTCCTCAGAGAGCAGGCCCTTCCGACGCCCATCCAGTCATC
ACCCCGTCACGGGCCTCAGAGAGCAGGCCCTTCCGACGCCCATCCAGTCATC
GTCACGGGCCTCAGAGAGCAGGCCCTTCCGACGCCCATCCAGTCATCACCCGT
GGTCCCCGGGATCTGATGTCACTCTCCTCGCTGAAGCCCTGGTACTGTCACAAACATCGAG
GTTATTAATTGCAAGCATCACAGAAATAGAAACAACAATTCCAGCATCCCTGGGCCTCAGA
CATAGATCTCATCCCCACGGAAGGGGTGAAGGCCTCGTCCACCTCGATCCACCAGCTCTGC
CTGACTCCACTGAAGCAAAACACACATCACTGAGGTACAGCCTCTGCCGAGACCCGT
ACAGCCGGCACCACAGAGTCAGCTGCACCTCATGCCACGGTGGGACCCACTCCCCACTAA
CAGGCCACAGAAAGAGAAGTGAAGCAGCACCCGGGCCACGACCCCTCAGTGGAGCTGGTCA
CAGTTAGCAGGAATCCCCTGGAAGAAACCTCAGCCCTCTGTTGAGACACCAAGTTACGTC
AAAGTCTCAGGAGCAGCTCCGGTCTCCATAGAGGCTGGTCAGCAGTGGCAAAACAACCTC
CTTGCTGGAGCTTGCTTCCCTACAGCCCTCGGAAGCCGCCCTCAAGAACCTCACCC
CTTCAGAGACACCGACCATGGACATCGAACCAAGGGGCCCTCCCCACCAGCAGGGACCC
CTTCCTCTGTCCTCCGACTACAACCAACAGCAGCCGAGGGACGAACAGCACCTTAGCAA
GATCACAAACCTCAGCGAAGACCAACGATGAAGCCCCAACAGCCACGCCACGACTGCCGGAC
GAGGCCGACCACAGACG**TGAG**TGCAGGTGAAATGGAGGTTCCCTCCCTGCGGCTGAGTG
TGGCTCCCCGGAAAGACCTCACTGACCCAGAGTGGCAGAAAGGCTGATGCAAGCAGCTCCAC
CGGGAACTCCACGCCACGCCACTTCCAGGTCTCCTACTGCGTGTCAAGGAGAGGCTA
ACGGACATCAGCTGCAGCCAGGCATGTCCTATGCCAAAAGAGGGTGCTGCCCTAGCCTG
GCCCTCCACCGACAGACTGCAGCTGCCTACTGTGCTGAGAGGTACCCAGAAGGTTCCATG
AAGGGCAGCATGTCCAAGCCCCAACCCAGATGTGGCAACAGGACCCCTGCTCACATCCAC
CGGAGTGTATGTATGGGGAGGGCTTCACCTGTTCCAGAGGTGTCCTGGACTCACCTGG
CACATGTTCTGTGTTCAAGTAAAGAGAGACCTGATCACCCATCTGTGCTTCCATCCTGCA
TTAAAATTCACTCAGTGTGGCCCAAAAAAAA

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FIGURE 326

MGCLWGLALPLFFFCEVGVSGSSAGPSTRRADTAMTTDDTEVPAMTLAPGHAALETQTLSA
ETSSRASTPAGPIPEAETRGAKRISPARERSFTKTSPNFMVLIATSVETSAASGSPEGAGM
TTVQTITGSDPEEAIFDTLCTDDSSEEAKTLTMDILTLAHTSTEAKGLSSESSASSDGPHPV
ITPSRASESSASSDGPHPVITPSRASESSASSDGPHPVITPSWSPGSDVTLLAEALVTVTNI
EVINCSITEIETTSSIPGASDIDLIPTEGVKASSTS DPPALPDSTEAKPHITEVTASAETL
STAGTTESAAPHATVGTPLPTNSATEREVTAPGATTLSGALVTVRNPLEETSALS VETPSY
VKVSGAAPVSI EAGSAVGKTTSFAGSSASSYSPSEAALKNFTPSETPTMDIATKGPFP TS RD
PLPSVPPTTNSSRGTNSTLAKITTSAKTTM KPQQPRPRLPGRGRPQT

N-glycosylation sites:

amino acids 252-256, 445-449, 451-455

cAMP-and cGMP-dependent protein kinase phosphorylation site.

amino acids 84-90

Casein kinase II phosphorylation sites.

amino acids 37-41, 108-112, 131-135, 133-137, 148-152, 165-169,
246-250, 254-258, 256-260, 269-273, 283-287, 333-337, 335-339,
404-408, 414-418, 431-435

N-myristoylation sites.

amino acids 2-8, 19-25, 117-123, 121-127, 232-238, 278-284, 314-
320, 349-355, 386-392, 397-403, 449-455

ATP/GTP-binding site motif A (P-loop).

amino acids 385-393

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FIGURE 327

GC GGAGCATCCGCTCGGGCCTCGCCGAGACCCCCCGCGGGATTGCCGGCTTCCCGGG
GCGCGACAGAGCTGCTCGCACCTGGATGGCAGCAGGGCGCCGGGCTCTCGACGCCA
GAGAGAAATCTCATCATCTGTGCAGCCTCTAAAGCAAACATAAGACCAGAGGGAGGATTAT
CCTGACCTTGAAGACAAAACATAAGTAAATTAAA**ATGTTCTCGGGGAGAAGGGAG**
CTTGACTTACACTTGGTAATAATTGCTCCTGACACTAAGGCTGTCAGTCAGAATT
GCCTCAAAAGAGTCTAGAAGATGTTGTCATTGACATCCAGTCATCTCTTAAGGGAATC
AGAGGCAATGAGCCCGTATATACTTCAACTCAAGAAGACTGCATTAAATTCTGCTGTTCAAC
AAAAACATATCAGGGGACAAAGCATGTAATTGATGATCTCGACACTCGAAAAACAGCTA
GACAACCCACTGCTACCTATTCTGCTCCAACGAGGAAGCCTGTCATTGAAACACAGCA
AAAGGACTTATGAGTTACAGGATAATTACAGATTTCCATCTTGCACAGAAATTGCCAAG
CCAAGAGTTACCCAGGAAGATTCTCTTACATGGCAATTTCACAAGCAGTCACTCCCC
TAGCCCACATCACACAGATTATCAAAGCCCACCGATATCTCATGGAGAGACACACTTCT
CAGAAGTTGGATCCTCAGATCACCTGGAGAAACTATTAAAGATGGATGAAGCAAGTGCCA
GCTCCTGCTATAAGGAAAAGGCCATTCTCAGAGTTACAATTTCCTCTGATCAAGAAA
TAGCTCATCTGCTGCCGAAATGTGAGTGCCTCCAGCTACGGTGGCAGTTGCTTCTCCA
CATACCACCTCGGCTACTCCAAAGCCCACCCCTTACCCACCAATGCTCAGTGACACC
TTCTGGGACTTCCCAGGCCACAGCTGGCCACCACAGCTCCACCTGTAACCACGTCACTTCTC
AGCCTCCCACGACCCCTCATTCTACAGTTTACACGGCTCGGCTACACTCCAAGCAATG
GCTACAACAGCAGTTCTGACTACCACCTTCAGGCACCTACGGACTCGAAAGGCAGCTTAGA
AACCATACCGTTACAGAAATCTCAAACTTAACATTGAAACACAGGAATGTGATAACCTA
CTGCACTTTCTATGTCAAATGTGGAGTCTTCACTATGAATAAAACTGCTTCTGGGAAGGT
AGGGAGGCCAGTCCAGGCAGTTCTCCAGGGCAGTGTCCAGAAAATCAGTACGGCCTTCC
ATTGAAAATGGCTCTATCGGGTCCCTGCTTTGGTGTCTGTTCTGGTGTAGGCC
TCGTCCTCTGGTAGAACCTTCGGAATCACTCCGCAAGGAAACGTTACTCAAGACTGGAT
TATTGATCAATGGGATCTATGTGGACAT**CTAAGGATGGAAC**CTCGGTCTCTTAATTCTT
TAGTAACCAGAAGCCAAATGCAATGAGTTCTGCTGACTTGCTAGTCTTAGCAGGAGGTTG
TATTGAAAGACAGGAAATGCCCTCTGCTTTCTTTGGAGACAGAGCTT
GCTCTGTTGCCAGGCTGGAGTGCAGTAGCACGATCTGGCTCTCACCGCAACCTCCGTCTC
CTGGGTTCAAGCGATTCTCTGCCCTAGCCTCTAAGTATCTGGGATTACAGGCATGTGCCA
CCACACCTGGGTGATTTGTATTTAGTAGAGACGGGTTTACCATGTTGGTCAGGCTG
GTCTCAAACCTGACCTAGTGTACCCACCTCTCGGCTCCAAAGTGTGGGATTACAGG
CATGAGCCACCACAGCTGGCCCCCTCTGTTTATGTTGGTTTTGAGAAGGAATGAAGTG
GGAACCAAATTAGGTAATTTGGTAATCTGTCATAAAATATTAGCTAAAACAAAGCTCT
ATGTAAGTAATAAAGTATAATTGCCATATAAAATTCAAACACTGGCTTATGCAA
GAAACAGGTTAGGACATCTAGGTTCCAATTCAATTCTGGTCCAGATAAAATCAAC
TGTTTATATCAATTCTAATGGATTGCTTTCTTTATATGGATTCTTAAACTTATT
CCAGATGTAGTCCTCAATTAAATATTGAATAATCTTGTACTCAA

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FIGURE 328

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><subunit 1 of 1, 431 aa, 1 stop
><MW: 46810, pI: 6.45, NX(S/T): 6
MFFGGEGSLTYTLVIICFLTLRLSASNCLKSLEDVVIDIQSSLSKGIRGNEPVYTSTQED
CINSACCSTKNISGDKACNLMIFDTRKTARQPNCYLFFCPNEEACPLKPAKGLMSYRIITDFP
SLTRNLPSQELPQEDSLLHGQFSQAVTPLAHHHTDYSKPTDISWRDTLSQKFGSSDHLEKLF
KMDEASAQLLAYKEKGHSQSSQFSSDQEIAHLLPENVSALPATVAVASPHHTSATPKPATLL
PTNASVTPSGTSQPQLATTAPPVTTVTSQPPPTLISTVFTRAAATLQAMATTAVLTTTFQAP
TDSKGSLETIPFTEISNLTNTGNVYNPTALSMSNVESSTMNKTAWEGRASPGSSSQGSV
PENQYGLPFEKWLLIGSLLFGVLFLVIGLVLLGRILSESLRRKRYSRLDYLINGIYVDI
```

Signal sequence.

amino acids 1-25

Transmembrane domain.

amino acids 384-405

N-glycosylation sites.

amino acids 72-76, 222-226, 251-255, 327-331, 352-356

cAMP- and cGMP-dependent protein kinase phosphorylation site.

amino acids 415-419

Tyrosine kinase phosphorylation site.

amino acids 50-57

N-myristoylation sites.

amino acids 4-10, 48-54, 315-321

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FIGURE 329

CTCCCACGGTGTCCAGCGCCAGAATGCGGCTTGGTCTGCTATGGGTTGCCTGCTGCT
CCCAGGTTATGAAGCCCTGGAGGGCCCAGAGGAATCAGCGGTTCGAAGGGGACACTGTGT
CCCTGCAGTGCACCTACAGGGAAAGAGCTGAGGGACCACCGGAAGTACTGGTGCAGGAAGGGT
GGGATCCTCTCTCGCTGCTGGCACCATCTATGCAGAAGAAGAAGGCCAGGAGACAAT
GAAGGGCAGGGTGTCCATCCGTGACAGCGCCAGGAGCTCTGCTCATTGTGACCCTGTGGA
ACCTCACCTGCAAGACGCTGGGAGTACTGGTGTGGGTCGAAAAACGGGGCCCCGATGAG
TCTTTACTGATCTCTGTTCGTCTTCAGGACCTGCTGTCCTCCCTCCCTCCAC
CTTCCAGCCTCTGGCTACAACACGCCTGCAGCCAAGGCAAAAGCTCAGCAAACCCAGCCCC
CAGGATTGACTTCTCTGGCTCTACCCGGCAGCCACCACAGCCAAGCAGGGGAAGACAGGG
GCTGAGGCCCTCCATTGCCAGGGACTTCCCAGTACGGGACGAAAGGACTTCTCAGTACAC
AGGAACCTTCCTCACCCAGCAGCCTCTCCTCTGCAGGGAGCTCCGCCCCCATGCAGC
TGGACTCCACCTCAGCAGAGGGACACCAGTCCAGCTCAGCAGTGGCAGCTCTAAGCCCAGG
GTGTCCATCCCGATGGTCCGCATACTGGCCCCAGTCCTGGTGTGTCAGCCTCTGTGAGC
CGCAGGCCTGATGCCCTCTGCAGCCACCTGCTCTGTGGAGAAAGGAAGCTAACAGGCCA
CGGAGACACAGAGGAACGAGAAAGTTCTGGCTCTCACGCTGACTGCGGAGGAAAAGGAAGCC
CCTTCCCAGGCCCTGAGGGGACGTGATCTCGATGCCCTCCACACATCTGAGGAGGA
GCTGGGCTTCGAAGTTGTCTCAGCGTAGGGCAGGAGGCCCTCTGGCCAGGCCAGCAGT
GAAGCAGTATGGCTGGCTGGATCAGCACCGATTCCGAAAGCTTCCACCTCAGCCTCAGAG
TCCAGCTGCCCGGACTCCAGGGCTCTCCCCACCCCTCCCCAGGCTCTCCTTGCATGTTCA
GCCTGACCTAGAAGCGTTGTCAGCCCTGGAGGCCAGAGCGGTGGCCTTGCTCTCCGGCTG
GAGACTGGGACATCCCTGATAGGTTCACATCCCTGGCAGAGTACCAAGGCTGCTGACCTCA
GCAGGGCCAGACAAGGCTCAGTGGATCTGGTCTGAGTTCAATCTGCCAGGAACCTCTGGC
CTCATGCCAGTGTGGACCCCTGCCCTCCACTCCAGACCCCCACCTGTCTTCCCTCCC
TGGCGTCCCTCAGACTTAGTCCCACGGTCTCCTGCATCAGCTGGTGTGAAGAGGGAGCATGCT
GGGGTGAGACTGGGATTCTGGCTCTTTGAACCACTGCATCCAGCCCTTCAGGAAGCCT
GTAAAAAACGTGATTCTGGCCCCACCAAGACCCACCAAAACCATCTCTGGGCTTGGTGCAG
GACTCTGAATTCTAACATGCCAGTGAATGTCGCACTTGAGTTGAGGGCCAGTGGCCTG
ATGAACGCTCACACCCCTCAGCTTAGAGTCTGCATTGGCTGTGACGTCTCACCTGCC
CAATAGATCTGCTCTGTCTGCAGCACCCAGATCCACGTGGGACTCCCTGAGGCCCTGCTAAG
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AAACCTGGCTCTTCTGTCTGGAAAGGGTACTTGCCTATGGGTCTGGTGGCTAGAGA
GAAAAGTAGAAAACCAGAGTGCACGTAGGTGTCAACACAGAGGAGAGTAGGAACAGGGCGG
ATACCTGAAGGTGACTCCGAGTCCAGGCCCTGGAGAAGGGTGGGGTGGTAAAGTA
GCACAACTACTATTTTTCTTCCATTATTGTTTTAAGACAGAATCTGTGCT
GCTGCCAGGCTGGAGTGCAGTGGCACGATCTGCCTCCAGGCTCTGGGTTCAAGTGA
CTTCTGCCTCAGCCTCCGAGTAGCTGGGATTACAGGCACGCCACACCTGGCTAATT
TTTGTACTTTAGTAGAGATGGGTTTACCATGTTGCCAGGCTGGCTTGAACCTGT
CTCAAAATGAGCCTCTGCTTCAGTCTCCAAATTGCCGGATTACAGGCATGAGCCACTGT
TCTGGCCCTATTCCTTAAAAGTGAATTAAAGAGTTGTTCAAGTATGCAAAACTGGAAAG
ATGGAGGAGAAAAGAAAAGGAGAAAAAAATGTCACCCATAGTCTCACCAGAGACTATCAT
TATTTCGTTTGTGACTTCCTCCACTCTTCTTCACTAATTGCCGGTGTCTT
TTTACAGAGCAATTATCTGTATATAACACTTGTATCCTGCCCTTCCACCTTATCGTTCC
ATCACTTTATTCCAGCACTTCTGTGTTTACAGACCTTTATAAAATGTTCATCA
GCTGCATAAAAAAA

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FIGURE 330

```
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<subunit 1 of 1, 332 aa, 1 stop
<MW: 36143, pI: 5.89, NX(S/T): 1
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GTIYAAEEGQETMKGRVSIRDSRQELSLIVTLWNLTLQDAGEYWCGVKEKGPDESLLISLFV
FPGPCCPPSPSPTFQPLATTRILQPKAKAQQTQPPGLTSPGLYPAATTAKQGKTGAEAPPLPG
TSQYGHERTSQYTGTSPHPATSPPAGSSRPPMQLDSTAEDTSPALSSGSSKPRVSIPMVRIL
LAPVLVLLSLLSAAGLIAFCSHLLWRKEAQQATEQRNEKFWLSRLTAEEKEAPSQAPEGDV
VISMPPLHTSEEELGFSKFKVSA
```

Important features:**Signal peptide:**

amino acids 1-17

Transmembrane domain:

amino acids 248-269

N-glycosylation site.

amino acids 96-99

Fibrinogen beta and gamma chains C-terminal domain.

amino acids 104-113

Ig like V-type domain:

amino acids 13-128

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/08439

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	C12N15/12	C07K14/47	C07K14/705	C12N15/62	C07K16/18
	G01N33/53	A61K38/17			

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K G01N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

STRAND

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 39448 A (HUMAN GENOME SCIENCES INC) 11 September 1998 (1998-09-11) see passages relating to gene 174 (clone H2MBF44) and the claims. ---	1-28
X	WO 98 42741 A (GENETICS INST) 1 October 1998 (1998-10-01) see passages relating to clone ck181_7 and the claims. ---	1-28
A	EP 0 834 563 A (SMITHKLINE BEECHAM CORP) 8 April 1998 (1998-04-08) the whole document ---	
A	WO 97 07198 A (GENETICS INST) 27 February 1997 (1997-02-27) the whole document ---	
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
16 August 2000	13.11.00
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl. Fax: (+31-70) 340-3016	Authorized officer Smalt, R

C(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>YOKOYAMA-KOBAYASHI M ET AL: "A signal sequence detection system using secreted protease activity as an indicator" GENE, NL, ELSEVIER BIOMEDICAL PRESS. AMSTERDAM, vol. 163, no. 2, 3 October 1995 (1995-10-03), pages 193-196, XP004041983 ISSN: 0378-1119 the whole document</p> <p>---</p>	
A	<p>KLEIN R D ET AL: "Selection for genes encoding secreted proteins and receptors" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, US, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, no. 93, 1 July 1996 (1996-07-01), pages 7108-7113, XP002077277 ISSN: 0027-8424 the whole document</p> <p>---</p>	
P,X, L	<p>WO 99 63088 A (BAKER KEVIN ;CHEN JIAN (US); GENENTECH INC (US); YUAN JEAN (US); G) 9 December 1999 (1999-12-09) see passages relating to PR0281 and the claims. L: priority.</p> <p>---</p>	1-28
P,X	<p>WO 99 46375 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 16 September 1999 (1999-09-16) see whole document, particularly passages relating to seq.ID'2 219 and 251</p> <p>---</p>	1-13, 17-28
P,X	<p>WO 99 53040 A (SCHMITT ARMIN ;SPECHT THOMAS (DE); DAHL EDGAR (DE); HINZMANN BERND) 21 October 1999 (1999-10-21) page 1 -page 8 see claims. page 128</p> <p>---</p>	1-13, 17-22, 24-28
P,X	<p>WO 00 08145 A (NOVARTIS ERFINDUNGEN VERWALTUNG ;NOVARTIS AG (CH); HOLNESS CLAIRE L) 17 February 2000 (2000-02-17) the whole document</p> <p>---</p>	1-13, 21-28
P,X	<p>WO 99 63083 A (TSURITANI KATSUKI ;ARASE SEIJI (JP); IKEDA AKIKO (JP); TAISHO PHAR) 9 December 1999 (1999-12-09) abstract see sequences.</p> <p>-----</p>	1-13,21, 22,25-28

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 00/08439

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple Inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Claims 1-28, All partially.

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: Invention 1: claims 1-28, all partially

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0281 (seq.ID.2), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0281, chimeric protein comprising a portion corresponding to PR0281, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto.

2. Claims: Inventions 2-132: claims 1-28,
all partially and claims 4 and 13 as far as
applicable

Subject matter as defined for invention 1 above, but limited to the respective amino acid sequences and corresponding nucleic acid sequences referred to as:

2. PR0276 (seq.ID's 5/6),
3. PR0189 (Seq.ID's 7/8),
4. PR0190 (Seq.ID's 13/14),
5. PR0341 (Seq.ID's 19/20),
6. PR0180 (Seq.ID's 22/23),
7. PR0190 (Seq.ID's 13/14),
8. PR0194 (Seq.ID's 27/28),
9. PR0203 (Seq.ID's 29/30),
10. PR0290 (Seq.ID's 32/33),
11. PR0874 (Seq.ID's 35/36),
12. PR0710 (Seq.ID's 40/41),
13. PR01151 (Seq.ID's 46/47),
14. PR01281 (Seq.ID's 51/52),
15. PR0358 (Seq.ID's 56/57),
16. PR01310 (Seq.ID's 61/62),
17. PR0698 (Seq.ID's 66/67),
18. PR0732 (Seq.ID's 72/73),
19. PR01120 (Seq.ID's 83/84),
20. PR0537 (Seq.ID's 94/95),
21. PR0536 (Seq.ID's 96/97),
22. PR0535 (Seq.ID's 98/99),
23. PR0718 (Seq.ID's 102/103),
24. PR0872 (Seq.ID's 112/113),
25. PR01063 (Seq.ID's 114/115),
26. PR0619 (Seq.ID's 116/117),
27. PR01188 (Seq.ID's 123/124),
28. PR0784 (Seq.ID's 134/135),
29. PR0783 (Seq.ID's 137/138),
30. PR0820 (Seq.ID's 145/146),

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

31. PRO1080 (Seq.ID's 147/148),
32. PRO1079 (Seq.ID's 150/151),
33. PRO793 (Seq.ID's 152/153),
34. PRO1016 (Seq.ID's 155/156),
35. PRO1013 (Seq.ID's 157/158),
36. PRO937 (Seq.ID's 159/160),
37. PR0842 (Seq.ID's 164/165),
38. PR0839 (Seq.ID's 166/167),
39. PR01180 (Seq.ID's 168/169),
40. PR01134 (Seq.ID's 170/171),
41. PR0830 (Seq.ID's 174/175),
42. PR01115 (Seq.ID's 176/177),
43. PR01277 (Seq.ID's 178/179),
44. PR01135 (Seq.ID's 180/181),
45. PR0828 (Seq.ID's 188/189),
46. PR01009 (Seq.ID's 193/194),
47. PR01007 (Seq.ID's 196/197),
48. PR01056 (Seq.ID's 198/199),
49. PR0826 (Seq.ID's 200/201),
50. PR0819 (Seq.ID's 202/203),
51. PR01006 (Seq.ID's 204/205),
52. PR01112 (Seq.ID's 206/207),
53. PR01074 (Seq.ID's 208/209),
54. PR01005 (Seq.ID's 210/211),
55. PR01073 (Seq.ID's 212/213),
56. PR01152 (Seq.ID's 215/216),
57. PR01136 (Seq.ID's 218/219),
58. PR0813 (Seq.ID's 220/221),
59. PR0809 (Seq.ID's 222/223),
60. PR0791 (Seq.ID's 224/225),
61. PR01004 (Seq.ID's 226/227),
62. PR01111 (Seq.ID's 228/229),
63. PR01344 (Seq.ID's 230/231),
64. PR01109 (Seq.ID's 235/236),
65. PR01383 (Seq.ID's 240/241),
66. PR01003 (Seq.ID's 245/246),
67. PR01108 (Seq.ID's 247/248),
68. PR01137 (Seq.ID's 249/250),
69. PR01138 (Seq.ID's 252/253),
70. PR01054 (Seq.ID's 255/256),
71. PR0994 (Seq.ID's 257/258),

3. Claim : 1

72. PR0812 (Seq.ID's 259/260),
73. PR01069 (Seq.ID's 261/262),
74. PR01129 (Seq.ID's 263/264),
75. PR01068 (Seq.ID's 265/266),
76. PR01066 (Seq.ID's 267/268),
77. PR01184 (Seq.ID's 269/270),
78. PR01360 (Seq.ID's 271/272),
79. PR01029 (Seq.ID's 273/274),
80. PR01139 (Seq.ID's 275/276),
81. PR01309 (Seq.ID's 277/278),

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

82. PRO1028 (Seq.ID's 280/281),
83. PRO1027 (Seq.ID's 282/283),
84. PR01107 (Seq.ID's 284/285),
85. PR01140 (Seq.ID's 286/287),
86. PR01106 (Seq.ID's 288/289),
87. PR01291 (Seq.ID's 290/291),
88. PR01105 (Seq.ID's 292/293),
89. PR0511 (Seq.ID's 294/295),
90. PR01104 (Seq.ID's 296/297),
91. PR01100 (Seq.ID's 298/299),
92. PR0836 (Seq.ID's 300/301),
93. PR01141 (Seq.ID's 302/303),
94. PR01132 (Seq.ID's 308/309),
95. PR01346 (Seq.ID's 313/314),
96. PR01131 (Seq.ID's 318/319),
97. PR01281 (Seq.ID's 325/326),
98. PR01064 (Seq.ID's 333/334),
99. PR01379 (Seq.ID's 339/340),
100. PR0844 (Seq.ID's 344/345),
101. PR0848 (Seq.ID's 346/347),
102. PR01097 (Seq.ID's 348/349),
103. PR01153 (Seq.ID's 350/351),
104. PR01154 (Seq.ID's 352/353),
105. PR01182 (Seq.ID's 356/357),
106. PR01155 (Seq.ID's 358/359),
107. PR01156 (Seq.ID's 360/361),
108. PR01098 (Seq.ID's 362/363),
109. PR01127 (Seq.ID's 364/365),
110. PR01126 (Seq.ID's 366/367),
111. PR01125 (Seq.ID's 368/369),
112. PR01186 (Seq.ID's 370/371),
113. PR01198 (Seq.ID's 372/373),
114. PR01158 (Seq.ID's 374/375),
115. PR01159 (Seq.ID's 376/377),
116. PR01124 (Seq.ID's 378/379),
117. PR01287 (Seq.ID's 380/381),
118. PR01312 (Seq.ID's 386/387),
119. PR01192 (Seq.ID's 388/389),
120. PR01160 (Seq.ID's 393/394),
121. PR01187 (Seq.ID's 398/399),
122. PR01185 (Seq.ID's 400/401),
123. PR01345 (Seq.ID's 402/403),
124. PR01245 (Seq.ID's 407/408),
125. PR01358 (Seq.ID's 409/410),
126. PR01195 (Seq.ID's 411/412),
127. PR01270 (Seq.ID's 413/414),
128. PR01271 (Seq.ID's 415/416),
129. PR01375 (Seq.ID's 417/418),
130. PR01385 (Seq.ID's 419/420),
131. PR01384 (Seq.ID's 423/424),
132. PR09828 (Seq.ID's 510/511).

For the sake of conciseness, the first subject matter is explicitly defined, the other subject matters are defined by analogy thereto.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

4. Claims: Invention 133: claims 1-36,69-74,99-102,
all partially and claims 4 and 13 as far as
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0943 (seq.ID.118), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PR0943, chimeric protein comprising a portion corresponding to PR0943, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa.

5. Claims: Inventions 134-136: claims 1-36,69-74,99-102,
all partially and claims 4 and 13 as far as
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR0183 (seq.ID.495), PR0184 (seq.ID.497) or PR0185 (seq.ID.499), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR0183, PR0184 or PR0185 through interaction with PR0943 and vice versa, method of linking a bioactive molecule to a cell expressing PR0943 using PR0183, PR0184 or PR0185 as binding ligands and vice versa, and method of modulating the activity of PR0943 by binding with PR0183, PR0184 or PR0185, and vice versa, whereby invention 134 is limited to PR0183, invention 135 is limited to PR0184, and invention 136 is limited to PR0185.

6. Claims: Invention 137: claims 1-28,37-44,75-80,103-106,
all partially and claims 4 and 13 as far as
applicable

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO331 (seq.ID.501), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PRO331, chimeric protein comprising a portion corresponding to PRO331, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO1133 through interaction with PRO331 and vice versa, method of linking a bioactive molecule to a cell expressing PRO331 using PRO1133 as binding ligands and vice versa, and method of modulating the activity of PRO331 by binding with PRO1133, and vice versa.

7. Claims: Invention 138: claims 1-28,37-44,75-80,103-106, all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO1133 (seq.ID.129), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO1133 through interaction with PRO331 and vice versa, method of linking a bioactive molecule to a cell expressing PRO331 using PRO1133 as binding ligands and vice versa, and method of modulating the activity of PRO331 by binding with PRO1133, and vice versa.

8. Claims: Invention 139: claims 1-28,45-52,81-86,107-110, all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO1387 (seq.ID.422), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PRO1387, chimeric protein comprising a portion corresponding to PRO1387, antibody against said protein, the isolated extracellular domain of said protein or a protein with at

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least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO363 or PRO5723 through interaction with PRO1387 and vice versa, method of linking a bioactive molecule to a cell expressing PRO1387 using PRO363 or PRO5723 as binding ligands and vice versa, and method of modulating the activity of PRO1387 by binding with PRO363 or PRO5723, and vice versa.

9. Claims: Invention 140 and 141: claims 1-28,45-52,81-86,
107-110,
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO363 (seq.ID.503) or PRO5723 (seq.ID.505), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO363 or PRO5723 through interaction with PRO1387 and vice versa, method of linking a bioactive molecule to a cell expressing PRO1387 using PRO363 or PRO5723 as binding ligands and vice versa, and method of modulating the activity of PRO1387 by binding with PRO363 or PRO5723, and vice versa, whereby invention 140 is limited to PRO363 and invention 141 is limited to PRO5723.

10. Claims: Invention 142: claims 1-28, 53-60,87-92,111-114,
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO1114 (seq.ID.183), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PRO1114, chimeric protein comprising a portion corresponding to PRO1114, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO3301 or PRO9940 through interaction with PRO1114 and vice versa, method of linking a bioactive molecule to a cell expressing PRO1114 using PRO3301 or PRO9940 as binding ligands and vice versa,

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and method of modulating the activity of PRO1114 by binding with PRO3301 or PRO9940, and vice versa.

11. Claims: Invention 143 and 144: claims 1-28, 53-60,87-92, 111-114,
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO3301 (seq.ID.507) or PRO9940 (seq.ID.509), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO3301 or PRO9940 through interaction with PRO1114 and vice versa, method of linking a bioactive molecule to a cell expressing PRO1114 using PRO3301 or PRO9940 as binding ligands and vice versa, and method of modulating the activity of PRO1114 by binding with PRO3301 or PRO9940, and vice versa, whereby invention 143 is limited to PRO3301 and invention 144 is limited to PRO9940.

12. Claims: Invention 145: claims 1-28,61-69,93-98,115-118,
all partially and claims 4 and 13 as far as applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PRO1181 (seq.ID.355), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to PRO1181, chimeric protein comprising a portion corresponding to PRO1181, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PRO7170, PRO361 or PRO846 through interaction with PRO1181 and vice versa, method of linking a bioactive molecule to a cell expressing PRO1181 using PRO7170, PRO361 or PRO846 as binding ligands and vice versa, and method of modulating the activity of PRO1181 by binding with PRO7170, PRO361 or PRO846, and vice versa.

13. Claims: Inventions 146-148: claims 1-28,61-69,93-98,

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115-118,
all partially and claims 4 and 13 as far as
applicable

Isolated nucleic acid having at least 80% sequence homology to a polynucleotide sequence encoding PR07170 (seq.ID.513), PR0361 (seq.ID.515) or PR0846 (seq.ID.517), vector comprising said nucleic acid, host cell comprising said vector, method of producing said protein using said host, isolated protein having at least 80% homology to said protein, chimeric protein comprising a portion corresponding to said protein, antibody against said protein, the isolated extracellular domain of said protein or a protein with at least 80% homology thereto, and said isolated protein lacking its signal peptide or a protein with at least 80% homology thereto. Method for detecting PR07170, PR0361 or PR0846 through interaction with PR01181 and vice versa, method of linking a bioactive molecule to a cell expressing PR01181 using PR07170, PR0361 or PR0846 as binding ligands and vice versa, and method of modulating the activity of PR01181 by binding with PR07170, PR0361 or PR0846, and vice versa, whereby invention 146 is limited to PR07170, invention 147 is limited to PR0361, and invention 148 is limited to PR0846.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9839448	A 11-09-1998	AU 6545398 A		22-09-1998
		EP 0972029 A		19-01-2000
		EP 0972030 A		19-01-2000
		WO 9839446 A		11-09-1998
WO 9842741	A 01-10-1998	AU 6777298 A		20-10-1998
		EP 0998490 A		10-05-2000
EP 0834563	A 08-04-1998	JP 10179178 A		07-07-1998
		US 5824504 A		20-10-1998
WO 9707198	A 27-02-1997	US 5707829 A		13-01-1998
		AU 6712396 A		18-02-1997
		AU 6768596 A		12-03-1997
		CA 2227220 A		06-02-1997
		CA 2229208 A		27-02-1997
		EP 0839196 A		06-05-1998
		EP 0851875 A		08-07-1998
		JP 11510045 T		07-09-1999
		US 6043344 A		28-03-2000
		WO 9704097 A		06-02-1997
		US 6074849 A		13-06-2000
		US 5969093 A		19-10-1999
WO 9963088	A 09-12-1999	AU 4328699 A		20-12-1999
		AU 2212299 A		26-07-1999
		WO 9935170 A		15-07-1999
WO 9946375	A 16-09-1999	DE 19811194 A		16-09-1999
WO 9953040	A 21-10-1999	DE 19817557 A		21-10-1999
WO 0008145	A 17-02-2000	AU 5730099 A		28-02-2000
WO 9963083	A 09-12-1999	JP 11332571 A		07-12-1999
		AU 3955099 A		20-12-1999